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LECTURES ON THE HEART

COMPRISING THE HERTER LECTURES, (BALTIMORE);
A HARVEY LECTURE, (NEW YORK)
AND AN ADDRESS TO THE FACULTY OF MEDICINE
AT McGILL UNIVERSITY, (MONTREAL).

BY

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PREFACE

The five lectures comprising this book were delivered during a brief visit to the American continent in the Autumn of 1914.

The Herter lectures were written to emphasise the advantages of intimately combining clinical and laboratory observations. Co-operation between wards and laboratories, as my visit has clearly taught me, is nowhere more freely or widely cultivated than in the Medical Schools of America. To these lectures, the Harvey lecture, which deals with questions of physiological interest, seems a fitting introduction. The address at Montreal serves to illustrate in a more extended manner the application of laboratory methods to questions of immediate and practical consequence.

It is a pleasure to acknowledge my indebtedness to the Committee of the Herter Foundation, and to the Harvey Society, who have kindly sanctioned the publication of the lectures in this form.

THOMAS LEWIS.

November 3rd, 1914.

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HARVEY LECTURE

ON

"THE EXCITATION WAVE IN THE HEART"

DELIVERED BEFORE THE HARVEY SOCIETY,

NEW YORK, OCTOBER 25TH, 1914.

Chapter I

THE EXCITATION WAVE IN THE HEART

Mr. President and Gentlemen,

May I preface what I have to say to-day by telling you how much I appreciate your invitation to deliver this Harvey lecture. How clearly the great physician, with whose name this Society associates itself, to whose name it delights to do honour, saw that the natural and safe advance of Medicine should follow its advance guard, physiology. Has he not fitly been named the Father of that Science? Is it not a matter of profound satisfaction and pride to us that this pioneer of experimental physiology should have been of our profession and that his greatest discovery should have been prompted by observations upon the human being? As Harvey by physiological study laid the foundation of Medicine as an exact science, so to-day, if we have learned the lesson which his writings should teach us, we shall maintain this tradition, preserving the closest intimacy between our conceptions of the physiology and pathology of mankind.

If we as students of the heart are exponents of such new methods as clinical electrocardiography, should we not in aspiring to become the humble disciples of this great teacher, first probe the normal phenomena of the heart's electric forces to the utmost? Can we who are met to emphasise the name and works of this man, for all time the first exponent of the heart's mechanism and function, more fittingly employ ourselves than by earnestly considering the natural heart beat? Gentlemen, in these questions you will find my reason for attempting to ex-

plain to you the origin and course of the natural excitation wave. Harvey our master chose as his illustration the heart of a King's deer; we his disciples may select a less regal beast, the dog.

General principles.

That the heart beat is accompanied by an electric discharge was first clearly shown by Kölliker and Müller in 1856. These workers laid upon the beating ventricle the nerve of a nerve muscle preparation, and noticed that at each contraction of the ventricle the nerve became excited. In that simple yet ingenious experiment our knowledge of the excitatory process commences. Since that time, a great number of workers have examined the mammalian ventricle from the point of view of the electric currents found in it. It will not be possible in this address to do justice to them, for the last chapters of the story are in themselves of undue length. I do not propose therefore to treat these questions historically, but to describe to you in language as simple as possible the results of recent observation. For some five years my laboratory has been engaged in the study of this question, and I have been joined in the work by a number of collaborators. These collaborators have been, for the most part, your countrymen, and it is a lively pleasure to me to know that several of them are here to-night. The Drs. Oppenheimer of this city published with me one of our first papers. Dr. Meakins of Montreal and Dr. White of Boston joined in these researches at a later date; and most recently I have had the help of Dr. Rothschild of Mt. Sinai Hospital.

Let us in the first place examine the electric events which are associated with the contraction of a simple strip of muscle, and formulate the general laws which are to guide us in our examination of so complex a structure as the heart. If we connect a simple strip of muscle, (*P-D*, Fig. 1) by means of non-polarisable electrodes to a sensitive galvanometer, and stimulate one end of this muscle (*P*), the galvanometer exhibits

two deflections. The meaning of these deflections, together forming when recorded a diphasic curve, is known. The first deflection accompanies the commencement of muscle activity in the neighbourhood of *P* (Fig. 1*a*), and this deflection has the same direction as has the deflection obtained when the zinc terminal of a copper-zinc couple replaces the active muscle *P*. *When muscle is active, therefore, it is in a state of relative negativity, in precisely the same sense that the zinc of a battery is relatively negative*. This negativity and the passage of a current from the inactive point through the galvanometer to the active point, produces the first swing of the string recorder, a swing which is upright in our curves. It is a large swing because it is unbalanced; the region of the other contact remaining for the time inactive. The second deflection of which I have spoken is due to similar conditions; it is produced after the excitatory process, associated with the contraction, has travelled in a wave from the proximal (*P*) to the distal end (*D*) of the muscle strip. *D* is active while at *P* activity has subsided (Fig. 1*d*). The portion of the muscle which has the electric charge of similar kind to our zinc terminal becomes transferred as the wave of activity passes from *P* to *D*. Consequently after the active process reaches *D* the swing of the galvanometer is reversed; a current passes from *P* through the galvanometer to *D*, and develops the second deflection which is

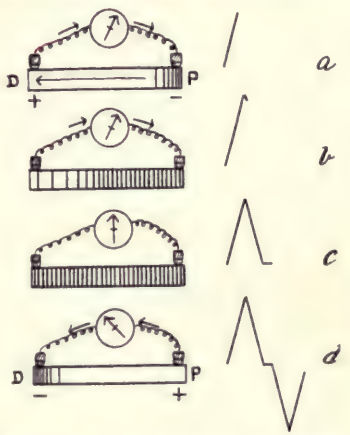


Fig. 1. A diagram, illustrating the development and subsidence of activity (and negativity) in a single muscle strip, responding to a stimulus applied at *P*. The corresponding and successive phases of the galvanometric curve are shown in the four lines *a*, *b*, *c* and *d*.

of opposite direction to the first. Thus the two phases of our recorded curve are due to a change in the relation of the active point to the two leading off contacts, and this change produces a reversal of direction, the two deflections together comprising a diphasic effect. The culmination of the first phase can be shown theoretically and experimentally to coincide with the arrival of the excitatory process at the distal end, in short strips of muscle (Fig. 1*b*). For when this occurs a balance begins to be established between the electric state under the two contacts. Evidently when the first phase is complete and the curve is about to cross the base line, activity is exactly equal under the contacts (Fig. 1*c*). Now this is a simple experiment and easily understood, once it is recognised that electrically active muscle is relatively negative to inactive muscle. Simple as it is, it is fundamental to electrocardiography; the whole of our interpretations are ultimately based upon it.

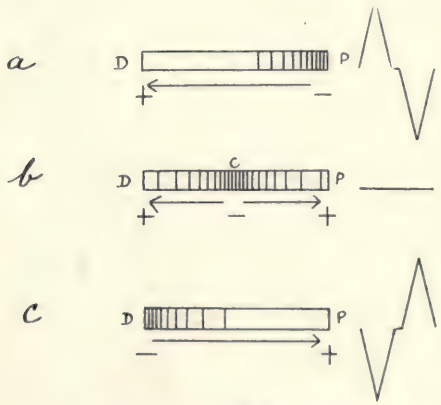


Fig. 2. A similar diagram, illustrating the inversion of the curve when the order of contraction is reversed, and its isopotentiality when the ends of the strip are activated simultaneously. The directions in which contraction is driven are indicated by the arrows.

It leads us immediately to our second law, which tells us that the *direction which the excitation wave takes, governs the form of the resulting curve.* And when I speak of excitation wave, you should recollect that this wave is intimately bound up with the contraction wave; it precedes it by an extremely short interval, and is presumably the result of those physico-chemical processes which at any point immediately precede actual contraction. That the

shape of our curve is governed by the direction of the wave is readily shown by our simple strip of muscle, for let us reverse the direction of contraction by stimulating the originally distal end (D), and forcing the wave to travel from D to P. We still obtain a diphasic curve; but compared with our first curve, each phase is now reversed in direction (Fig. 2*a* and *c*); it is easy to see why this is so, for having reversed the contraction, we have reversed the order in which the ends of the strip become relatively negative. But supposing that the same strip is stimulated at its centre point (Fig. 2*b*), and that the contraction wave travels with equal rapidity to the two ends, where our contacts are arranged. Each end then becomes negative at the same instant and the two effects neutralise each other.

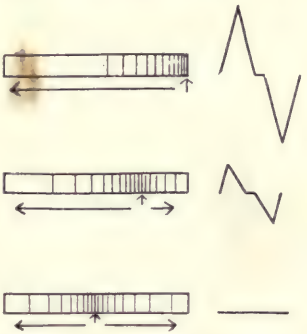


Fig. 3. A similar diagram; to show that maximal excursion of the galvanometric recorder is obtained when the interval of delay between the arrival of the excitation wave at the contacts is greatest.

In these circumstances there will be no swing of the recording instrument. Further, supposing that the excitation wave is started now at P and then at a series of regularly placed points up to a centre point (Fig. 3), then a graduated series of curves will be obtained, from a simple and large diphasic curve at one end of the scale, through curves of gradually diminishing amplitude, to a horizontal line at the other. From observations of this kind it is clear that the amplitude of the first phase is greatest when the time interval between the receipt of the excitation at the two contacts is greatest. If the time interval is nothing, a state of isopotentiality is established, and as the time interval is longer and longer, so the effects are more and more unbalanced, and the culmination, occurring later and later, has more and more opportunity to develope. When we deal with a

sheet of muscle, for example the auricle, as opposed to a strip, then the same statement applies; if a point is stimulated on the surface and a pair of contacts is arranged at a little distance away, then the amplitude is greatest when the contacts are radial * to the point of stimulation (Fig. 4*a*) for with these conditions the interval between the arrival of the wave at the two contacts is maximal.

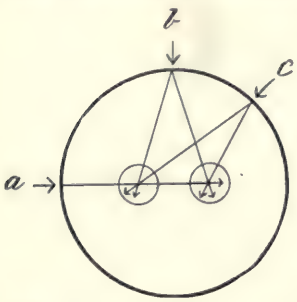


Fig. 4. The circle represents a sheet of muscle, excited at *a*, *b* or *c*, and examined at two central contact points. The excursion of the recorder is greatest when the contacts are in the line of the excitation wave; i.e., when the muscle is stimulated at *a;* it is least when stimulation is at *b*, for in this circumstance activity is simultaneously developed at the contacts.

In these observations we have the basis of our first investigations of the mammalian heart.

I. THE ORIGIN OF THE EXCITATION WAVE IN THE AURICLE.

The point which is relatively negative to all outlying ones.

If we place a pair of contacts upon a given area of the mammalian auricle and rotate them through an angle of 90 degrees, our curve varies in amplitude. We are able quickly to isolate a line which yields the greatest amplitude when the contacts are placed along it. Such lines are favourable lines from which to lead, and we may conclude that such lines approximately represent the lines along which the natural excitation wave travels. Such lines in the mammalian auricle converge to a point in the neighbourhood of the angle of superior vena cava and right appendix, where as you know the chief part of the sino-auricular node is situate. A specially favourable line is that of the tænia terminalis. We have, therefore,

* As Engelmann has shown the excitation wave radiates from a point of stimulation.

a preliminary evidence that the excitation wave radiates from a central position, the region of the angle named.

We take our second step. If the natural excitation wave spreads along radiating lines from the upper regions of the sulcus terminalis and we place one contact over this region and the other upon a circle of points surrounding it, we should, according to a rule which has been formulated, obtain a series of curves of good excursion, and, if activity is always developed under the central contact first, this contact should always be primarily negative to all other points. That is to say, if we

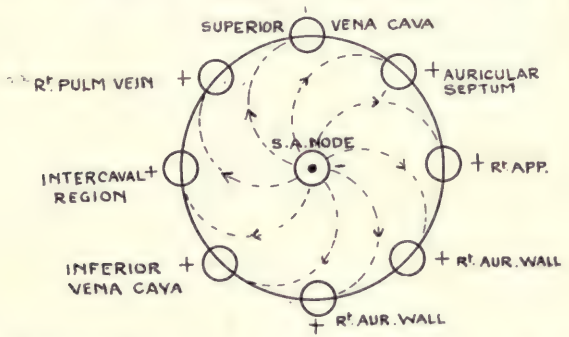


Fig. 5. A diagram, illustrating a method of examining a sheet of muscle. A central contact lies over the region giving rise to the excitation wave, the second contact is placed at outlying points successively. In these circumstances, the central contact always exhibits primary negativity.

make such radiating leads, maintaining our central contact upon the point at which the excitation wave arises, a series of curves should be obtained, of which the first phases are always of a given sign; the direction of the deflections should always indicate primary negativity of the central point (Fig. 5), *i.e.*, the first deflections should all be upright.

There is but one portion of the superficies of the mammalian auricle which exhibits these electric relations during normal contractions. If one contact is placed on the upper reaches of the sulcus terminalis and the other contact is moved along a

circumference surrounding this centre, it matters not where this second contact lies, the first deflection obtained with auricular systole is upward in direction, indicating relative negativity of the centre point. Such are the events when the centre contact lies in apposition to the head and superficial part of the sino-auricular node (Fig. 6). Now this experiment is a striking one, for the auricular muscle in this neighbourhood is thin, and the *S-A* node lies in what we may regard as the centre of a muscle sheet, that is to say, a complete circle of points may be arranged around it. There is little or no possibility that this region of the heart receives the excitation wave from some deeper structure, for all possible paths to the node may be investigated. The conclusion that this centre is the centre in which the excitation wave originates is most strongly suggested. The observations upon which this proposition rests were made by Wybauw and by observation in my laboratory in conjunction with the Drs. Oppenheimer. They are observations which I have repeatedly confirmed since our original publication, and which have been recently confirmed by Eyster and Meek, independent workers in this land.

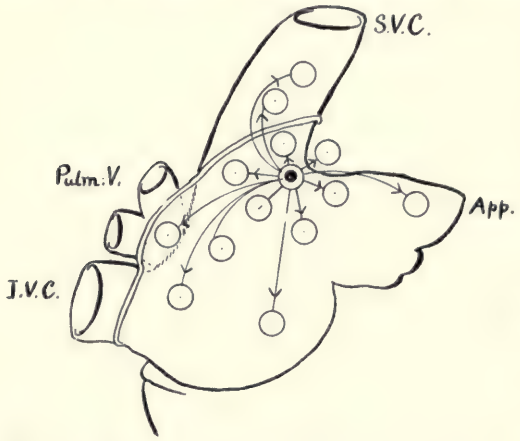


Fig. 6. The contacts as applied to an auricle. The central contact, which is invariably relatively negative to outlying points when activity in the auricle starts, overlies the *S.A.* node.

In the pig's heart, the sino-auricular node lies further up the sulcus than in the dog, and in one animal of this species I have

found the point of relative negativity to be in a corresponding position. It lay, as Ivy Mackenzie subsequently showed histologically, immediately over the sino-auricular node in this particular animal, as it had lain in all our dogs.

Forcing a natural excitation wave.

There is a second and distinct method of approaching the same subject. Suppose that we start contractions from various regions of the auricle and observe the type of curve which each

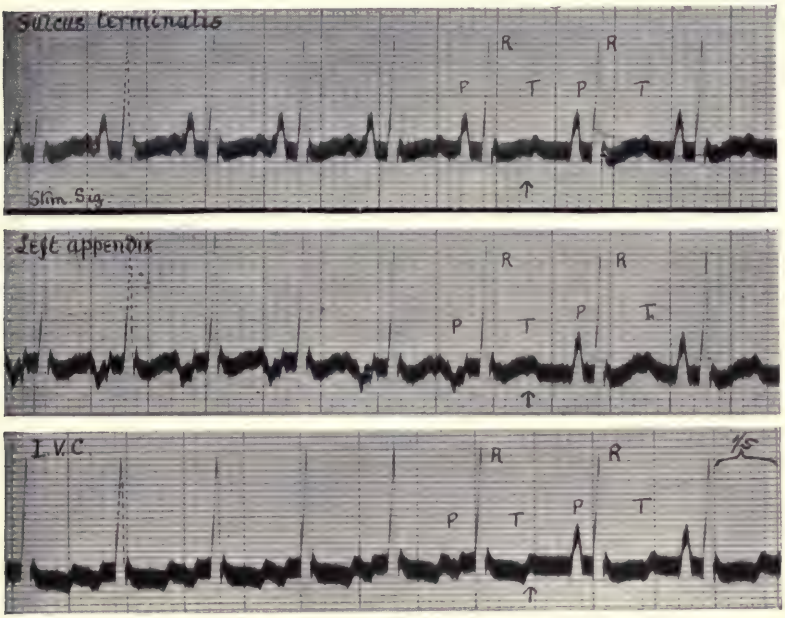


Fig. 7. Three electrocardiograms from a dog (Lead *II*). The last two cycles in each curve are natural heart beats. The remaining cycles are in response to stimulation over (1) the upper part of the sulcus terminalis, (2) left appendix, and (3) inferior cava. The natural beats are simulated when stimulation is in the region of the *S.A.* node.

yields, using a given and fixed lead, and compare such curves with those of the normal heart beat. I have said that the shape of the curves will be controlled by the direction which the ex-

citation wave takes in the muscle. If, as we stimulate the auricle to contract, we discover some region of it which yields curves which are identical with the normal, we may be sure that the natural excitation waves and those propagated from stimulation of the area in question follow similar paths. They can only follow similar paths if the region which we stimulate is the region from which the normal excitation waves are propagated. In the case of the mammalian auricle, as I have shown, there is but a single area which answers to these conditions (Fig. 7). It is the area immediately surrounding the upper reaches of the sulcus terminalis, the region which contains the *S-A* node. Our second evidence, therefore, accords with our first; both indicate the *S-A* nodal region as that in which the excitation wave has its birth.

Extrinsic and intrinsic deflections.

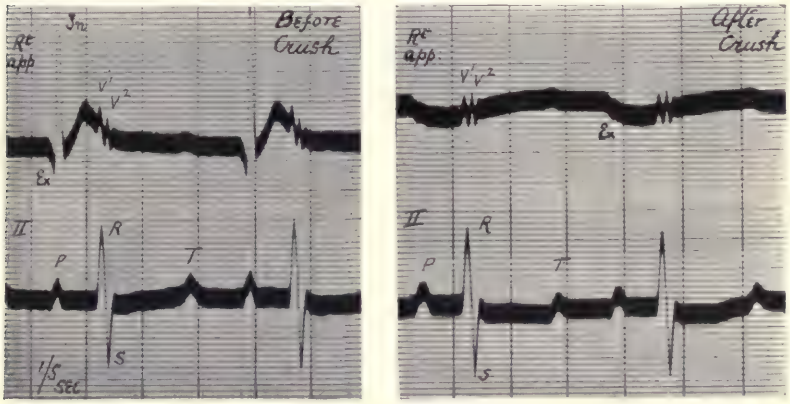
I pass to a consideration of what are termed "outlying leads," that is to say, leads in which neither contact lies over the *S-A* node. In leading directly from the heart muscle, the chief deflections are produced by the arrival of the excitatory process immediately beneath the contacts. The contacts are exposed to the full force of this electric discharge. Such leads are very different from those utilised in human electrocardiography, for in them the contacts are upon the limbs and not upon the heart. Curves of the excitation wave may be obtained under each condition, and for purposes both of description and of investigation, the direct and indirect effects should not be confused. Especially is this the case in leading from the heart itself. In such leads, the contacts lie on the muscle and the deflections are of two kinds.

1. There are deflections which result from the arrival of the excitation process immediately beneath the contacts; these we term *intrinsic deflections*. They are deflections, as you may

suppose, which represent considerable electrical potentials and have considerable amplitudes.

2. There are also deflections which are yielded by the excitation wave, travelling in distant areas of the muscle. To these we apply the term "*extrinsic deflections.*"

A simple example of intrinsic and extrinsic deflections is the following. Let us place two contacts upon the sulcus terminalis; at each beat of the auricle a large intrinsic deflection is



a *b*

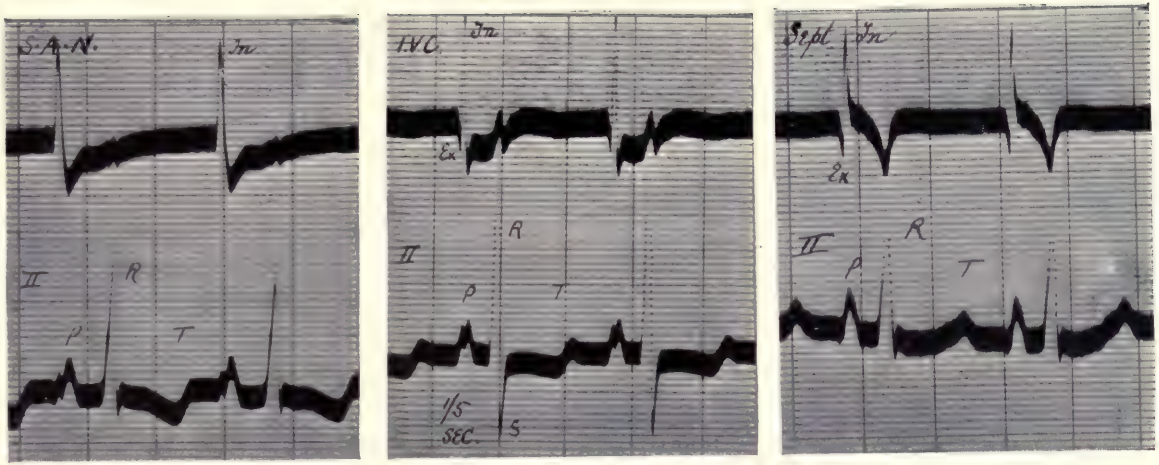
Fig. 8. Simultaneous electrocardiograms. The upper curves from the appendix, the lower curves from lead *II*. Showing the effect of crushing the base of the appendix and rendering the tissue under the contacts inactive. The chief or intrinsic deflection (*Tn*) is abolished; the extrinsic deflection (*Ex*) remains, as do the ventricular deflections (*v*).

produced by the arrival of the excitation wave beneath the nearest contact. When the ventricle contracts, the same contacts pick up smaller electric discharges from the last named chamber. These extrinsic effects are records of muscle activity at a distance. But the same double effect is noticed in the auricle itself. If we lead by two contacts from the right auricular appendix for example, we obtain a curve of the form shown in Fig. 8*a*. You see the usual tall spike, but it is pre-

ceded by a small downward deflection. That this initial deflection is not produced by activity in the appendix, and that the chief deflection is, can readily be demonstrated by crushing the base of the appendix. In this manner the appendix is rendered inactive, and when this is accomplished, the type of curve changes. The extrinsic effect, the small initial deflection, remains, while the intrinsic effects disappear (Fig. 8*b*). Now this is a fundamental demonstration, for it permits us to analyse those curves which are obtained from outlying leads. All such leads give curves of composite form; consisting of a main deflection, which corresponds to the arrival of the excitation process beneath the contacts, and diminutive initial deflections which are due to the passage of other portions of the auricular muscle into the excitatory state. In considering the course of the excitation wave, as opposed to its origin, we shall focus our attention upon these chief or intrinsic deflections, for they will alone concern us.

The point of primary negativity.

It has been said that a single point of the auricular muscle shows negativity relative to surrounding areas when the auricle first becomes active, and it has been concluded that this is so because this area first developes negativity or activity. Recently we have been able to demonstrate (Lewis, Meakins and White) that such is indeed the case by a direct and most conclusive method. We take simultaneous electrocardiograms (Fig. 9), either from two direct leads or preferably from a direct lead and a standard limb-lead (Lead *II*). By using exact methods of mensuration we have been able to reduce our customary error below a thousandth of a second and to measure the time of onset of the excitation wave, relative to *P* in the standard, in various regions of the auricle with great accuracy. Having searched the whole of the superficies of both auricles and the septum internally in a large number of animals, we can



a *b* *c*

Fig. 9. Examples of simultaneous electrocardiograms. The upper curves were taken from the region of the node, the inferior cava and the septum, respectively; the lower curves are from the right forelimb and left hind limb (Lead *II*) in each instance.

affirm that the first appearance of the excitation wave is over the head of the sino-auricular node and that it appears at later times in all other regions.

The same observations provide this and another important evidence that the *S-A* nodal region originates the excitation wave. It is the only region of the auricle from which curves are obtained, in which there are no initial deflections (Fig. 9*a*); the reason being that when the intrinsic deflection is obtained from this lead, the whole of the rest of the auricular tissue is in a state of inactivity; while in all outlying leads the intrinsic deflection, which represents activity, is preceded by initial movements of the string (Fig. 9*b* and *c*), which represent currents from the preceding activity of the *S-A* nodal region and surrounding areas.

I may sum up this the first part of my address to you, in the statement that we have abundant and conclusive evidence that the excitation wave commences in the immediate neighbourhood of the head of the sino-auricular node.

II. THE COURSE OF THE EXCITATION WAVE IN THE AURICLE.

When we examine the intrinsic deflections in curves from outlying leads, if the contacts are arranged radially to the *S-A* node, the direction of the intrinsic deflection is always the same, indicating that of the two contacts the proximal always receives the excitation wave first (Fig. 10); we have taken many hundreds of such curves without noting a single exception to this rule. From the direction of the intrinsic deflection alone we may conclude that the excitation wave spreads from the *S-A* node in all directions radially, that it runs down the tænia terminalis into the tip of the right appendix, along the intra-auricular band to the tip of the left appendix, and down the septum; that it runs into all the veins, caval, coronary and pulmonary, against the blood stream.

And these conclusions are completely substantiated by our

readings of the times at which the excitation wave reaches particular points. If a series of contacts is placed upon the auricle

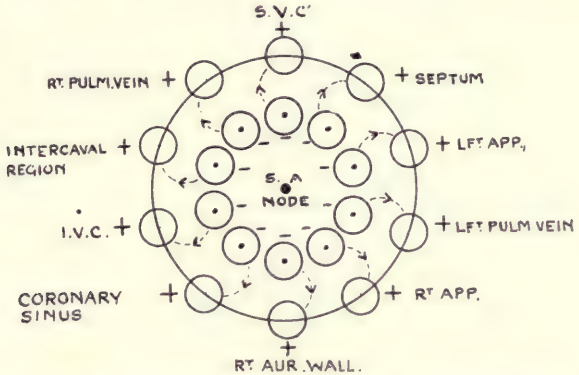


Fig. 10. A diagram illustrating a system of "outlying" leads. A pair of contacts is arranged radially to the node in various regions. The proximal contact always receives the excitation wave first, as shown by the direction of the intrinsic deflection.

in a direction radial to the *S-A* node, and the times at which the excitatory process arrives in each is estimated (Fig. 11 and

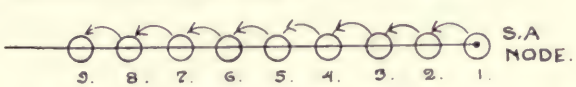


Fig. 11. A diagram illustrating leads from serial contacts. If the *S-A* node lies at one end of the series, the time at which the excitation wave appears recedes uniformly throughout the series, starting at the nodal end.

13), a contact proximal to the *S-A* node is always found to receive the excitation wave before a point more distal; and if the contacts are equidistant from each other, the times at which the excitation wave appears at the individual contacts of the series increase in a regular order. The excitation wave passes up the superior vena cava and flows along it to a point well outside the pericardium (Fig. 15); it ends where the heart muscle ends and the venous muscle begins. It passes down the

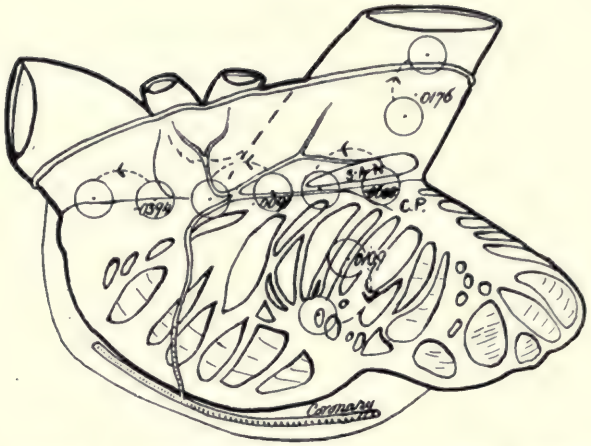


Fig. 12. Outline of an auricle in an actual experiment; showing the arrangement of the muscle bands; the concentration point (*C.P.*); and the outline of the *S.A* node. The diagram is accurately to scale, and illustrates the method of leading off by paired contacts and the subsequent orientation.

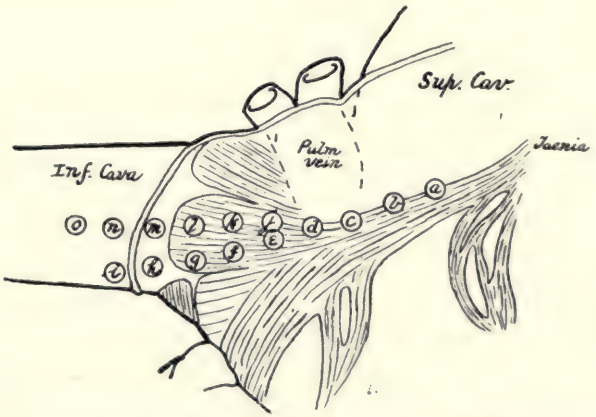


Fig. 13. A scale drawing from an actual experiment; showing a number of contacts used for leads from sulcus and inferior cava. Examples of the curves are shown in Fig. 14.

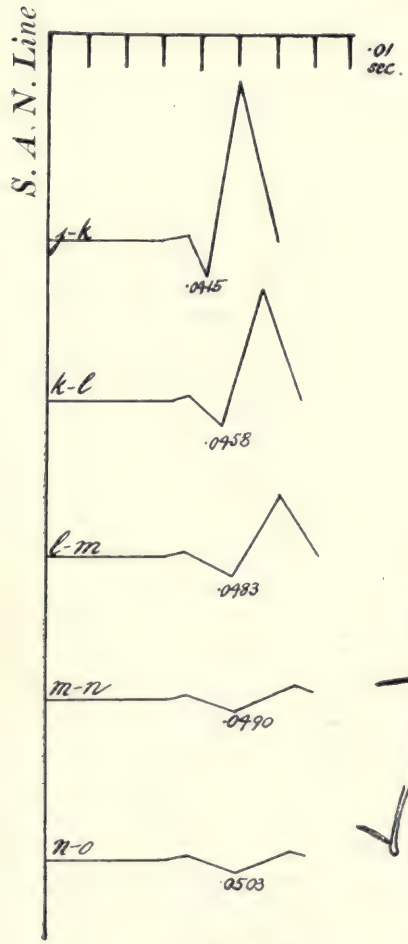
inferior cava to the edge of the cuff of muscle which is in places intrapericardial, in places extrapericardial (Figs. 13 and 15).

Knowing the distances between our contacts and the *S-A* node, we are able to estimate the rates of conduction of the wave to all parts of the auricle. The average transmission times, distances and rates are given in the accompanying table. The

Region.	Distance in mm.	Transmission Time.	Transmission Rate.	Number of Observations.
Intercaval	15.2	.0139	1232	18
Intra aur. Band	12.9	.0126	1252	6
S. V. C.	8.2	.0136	588	11
Septum (mid and low).	31.5	.0305	1059	11
Rt. app.	28.0	.0314	955	11
Rt. aur.	16.0	.0206	859	7
R. Pulm. V.	24.0	.0254	1121	4
I. V. C.	31.5	.0325	998	18
Cor. Sinus.....	43.9	.0412	1096	5
L. Pulm. V.....	45.2	.0412	1118	5
L. App.	44.6	.0446	996	7

Average heart rate 158.4.

transmission rates are wonderfully uniform from node to all parts of the auricle; such differences as occur are readily accounted for by small errors of measurement, or by the arrangement of the muscle bands, for it seems as if the rate of transmission is greatest where the muscle bands are straight. The solitary exception to the statement that the rate of transmission is uniform and approaches 1000 mm. per second is found in the superior cava; here it is lower and we are inclined to attribute this difference to the direction of the muscle fibres in this vein; they are arranged for the most part obliquely across the vein, while our transmission rates have been estimated up and down it. We are unable to obtain evidence of hindrance to the passage of the wave from node to auricle at any point; the



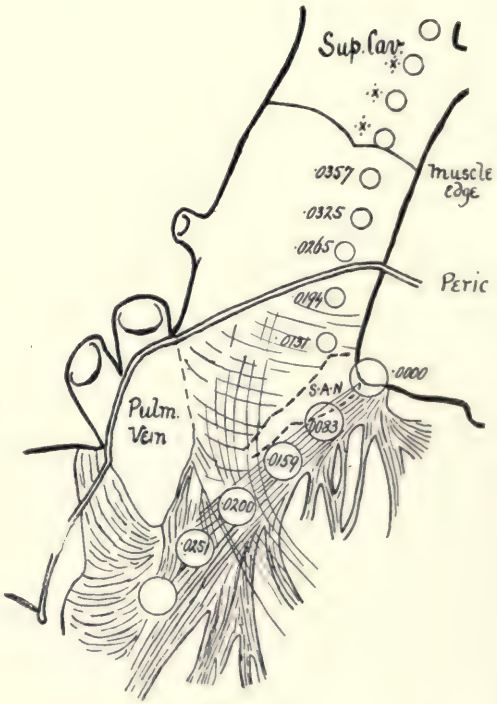


Fig. 14. Fig. 15.

Fig. 14. A diagram showing outlines of the curves obtained from 5 of the leads of Fig. 13. Charted in relation to the first appearance of the excitation wave in the auricle (*S.A.N.* line). The intrinsic deflection gradually recedes in time as the lead is taken lower on the vein, until the edge of the muscle is reached; the intrinsic deflection is then lost.

Fig. 15. Serial leads from sulcus and superior cava in another auricle. The times at which the excitation wave appeared at the several contact points are given. From the highest *S.V.C.* (contacts marked *) no intrinsic deflections were obtained.

rate of travel appears to be uniform, the direction of travel radial in all directions. Neither can we find any evidence of an increased rate of conduction to the *A-V* node, our calculated rates are the same for all parts of the auricular septum as for the rest of the auricular tissue. We have also used special methods of estimating the transmission time from node to node, by a method which I do not propose to consider in detail, and find it to be long.

The excitation wave in the auricle may be likened to the spread of a fluid poured upon a flat surface, its edge advances as an ever widening circle, until the whole surface is covered (Fig. 16); such variation as exists in the rate of travel along various lines in the auricle is fully accounted for by the simple anatomical arrangement of the tissue. If we examine the arrangement of the muscle bands of any mammalian auricle, we shall agree, I think, that they are ordered upon a definite plan. Immediately below the *S-A* node the fibres collect from all parts of the superficies of the right auricle in a curious fan shaped manner, to join in a knot of tissue which we term the *concentration point* (Fig. 12 *C. P.*). The *S-A* node is placed in the most advantageous position possible for a quick distribution of the contraction wave to all parts of the auricle, the fibres stream into this region of the heart from all the chief outlying regions.

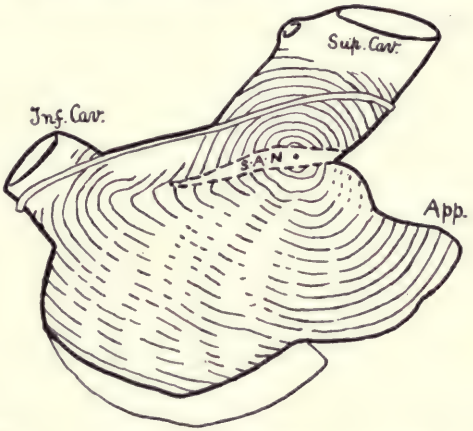


Fig. 16. A diagram illustrating the spread of the excitation wave over the surface of the right auricle. The spread is almost uniform and follows the chief muscle bands.

The chief fibres of the right appendix run direct to the head of the sulcus; the tænia runs from bottom to top of sulcus; the intra-auricular band runs from the angle across to the left appendix; other fibres run down the intra-auricular septum.

To sum up; the excitation wave, which has its origin in the *S-A* node spreads immediately and at rates ranging about 1000 mm. per second along the chief muscle tracts which radiate from the neighbourhood of this node; it courses throughout the whole of the auricular tissue, up to its ending upon the chief veins, and courses down the septum at a similar speed to reach the *A-V* node, whence it is transmitted to the ventricle. Is it not true to say that one auricle contracts before the other; the excitation wave appears in some portions of the right auricle before some portions of the left and vice-versa. The spread may be likened to the spread of fluid poured upon an almost flat surface.

III. THE EXCITATION WAVE IN THE VENTRICLE.

We have followed the course of the excitation wave from the sino-auricular node, throughout the auricle and to the auriculo-ventricular node. I do not propose to deal with the evidence for the transmission of the impulse from auricle to ventricle. We know as a result of recent investigations that it passes through the auriculo-ventricular bundle; and there is powerful evidence that it is distributed in the ventricle through that intricate and almost universal subendocardial network, the Purkinje system.

We pass to a study of the excitation process in the ventricle itself. In discussing this subject I propose to take a somewhat unusual course. At a somewhat later date it is proposed to publish a full paper on this subject; the work of Dr. Rothschild and myself is still in progress but is sufficiently advanced to bring before you in the form of a preliminary communication.

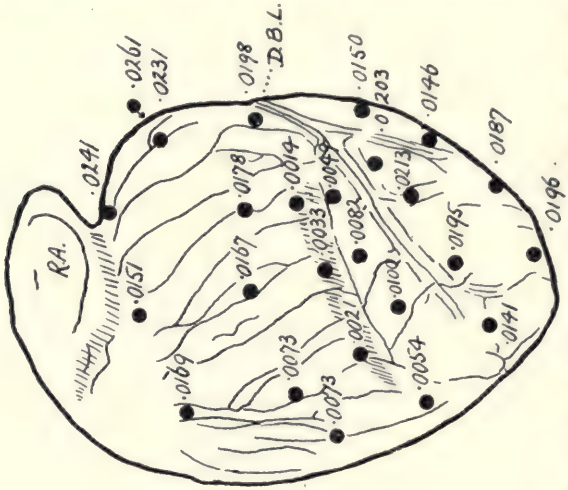
Our observations have been conducted along lines similar to those for the investigation of the auricle.*

We estimate the time of the appearance of the excitation wave, relative to *R* in a standard electrocardiogram, in the various areas of the musculature. The problems are more difficult than those connected with the auricle. In the last named chamber, as we have seen, the wave spreads in uniform and diverging lines. At an early stage of our observations we found that the spread in the ventricle happens in an entirely different fashion. If we examine a series of points upon a superficial band of ventricular muscle, for example, the conspicuous fibres which sweep from the conus across the upper part of the interventricular groove and around the left border of the heart to the apex, we immediately ascertain that the wave does not course along these bands.

Fig. 18 serves as an illustration: the excitation wave appears at a series of points along the right border of this diagram at time intervals, .0241, .0231, .0198, .0150, .0146, .0187 and .0196 sec. after *R*. It appears almost simultaneously at all these points, although they overlie the same muscle band. We have conclusive evidence that the excitatory process takes little or no consideration of the anatomical arrangement of the musculature of the ventricle. If we cover the front of the heart with contacts and estimate the order of the excitation process, we constantly discover an area in the region of the anterior attachment of the wall of the right ventricle (shaded area in Fig. 18) in which the excitatory process first commences so far as the superficies of the heart are concerned. But there is this remarkable fact; there exists in this region a considerable area, though it is of variable extent, in which the excitatory process commences almost simultaneously. If we examine the underlying structures we shall find that this

* With the exception that single contacts are placed on the ventricle while the second contact lies on the chest wall.

region is the most directly supplied by the right branch of the *A-V* bundle, and we have little doubt that the distribu-



Figs. 17 and 18. Outlines of the front of the heart in an actual experiment. Upon Fig. 17 arrows have been drawn; they depict the direction of spread on the front of this heart, investigated by means of closely paired contacts. Here the direction of the deflection was the index.

Fig. 18. The times at which the excitation wave appeared on the front of the same heart, related to the upstroke of *R* in lead *II*.

R.A. = Rt. appendix.

D.B.L. = Descending branch of left coronary artery.

tion of the right branch to this region is responsible, in part at least, for its early and simultaneous excitation. Examining the whole superficial surface of the heart in a number of ani-

mals, we find a close resemblance in the distribution from beast to beast. The superficial area which passes earliest into a state of excitation is almost always that which I have indicated, namely the portions of the conus where these join the interventricular groove. This is the portion of the wall overlying the large anterior papillary muscle of the right ventricle. The rest of the right ventricle becomes active later; the latest region is the upper wall of the conus directly below the pulmonary valves; the base of the right ventricle at its fusion with the fat in the *A-V* groove, and that portion which lies along the posterior interventricular groove, is almost but not quite so late.

Yet although there is this almost constant order, the time differences between the onsets of activity in the several parts of the right ventricle are remarkably small. In the case of the auricle, the wave takes from start to finish 4 to 5 hundredths of a second to complete its course. In the ventricles, although these chambers are so much larger, the whole course is usually completed in dogs of the same size in less than 3 hundredths of a second.

The order in the left ventricle is equally definite, though at present I shall not enter into detail. The earliest point is the vortex of the left ventricle or the extreme apex, and this region sometimes successfully rivals the right ventricle in the race; a hundredth of a second later the neighbouring points are activated. The appearance of activity over the remainder of this chamber is practically simultaneous, the time differences are usually to be measured in a few thousandths of a second. The basal attachment is generally speaking latest of all and practically coincident with the activity in the conus region.

No system of spread from point to point of the muscle fibres in a definite order can be imagined which will explain this distribution. We are forced to assume that the ventricular wall is reached by an impulse travelling along a large number

of paths of distribution. These paths as we are able to show are the Purkinje paths. If we examine a series of points, such as those shown in Fig. 19 before and after section of the right branch of the *A-V* bundle we find clear evidence for this statement. After section of this branch, as you are aware, a conspicuous change occurs in the form of the axial electrocardiogram; this change interferes to some extent with our absolute standard of measurement, but we are able to ascertain the relative order before and after the interference with precision. It is found that prior to section the right ventricle becomes active before the left in such a series of contacts as is figured; but after section the order changes. The relation of points to each other over the left ventricle remains unaltered; while activity in the right ventricle is materially delayed and progresses from left towards right. The Purkinje system is thus proved to be concerned in the distribution. But allowing this to be the case, we have still to explain a great deal.

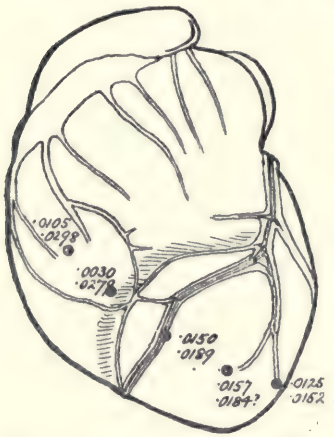


Fig. 19. Outline of the front of a dog's heart, upon which five contact points were investigated, before (top figures) and after (bottom figures) section of the right branch of the *A-V* bundle. It will be noted that over the left ventricle the order remains unchanged; but over the right, whereas before section the excitation wave appeared earliest in this region, after section it appeared latest.

Even where we take into account this branching system, we cannot fully explain the time relations over certain regions unless we assume that ventricular conduction is much more rapid than conduction in the auricle. To take an example: there are no free branching strands to the region of the conus; the subendocardial network in this region is spread as a continuous sheet;

yet conduction to the muscle beneath the pulmonary valves is extremely rapid. To meet these difficulties of explanation we have devised special experiments. It has been necessary to measure the rate of conduction through various tissue areas when an *artificial* excitation wave is propagated across contacts in line with each other. The natural rate of conduction in the auricle is fairly uniform and at about 1000 mm. for a second. The rate of conduction in the ventricle varies with the region examined. *It is highest and approaches or surpasses 2000 mm. per second where the muscle is thinnest.* It is lowest and approaches 400 mm. per second where the muscle is thickest. The reason for this variation is clear to us. The rate of conduction through ventricular muscle is slow, the rate of conduction through Purkinje substance is approximately at least 5 times as fast. When we excite the pericardial surface, the difference in the times at which the excitation wave reaches the contacts in line with the stimulation point, depends upon whether the excitation wave has time to travel through and into the Purkinje substance and along it and out again through the muscle to our contacts, before it passes directly to our contacts through the muscle alone. Evidently the thicker the tested muscle, the less likelihood is there of quick penetration. That this explanation is valid is clearly shown by two further experiments.

If two contacts are placed opposite to each other, one on the pericardial, the other upon the endocardial surface, the natural excitation wave always reaches the internal contact first (Fig. 20). It also reaches the internal contact first, *and by precisely the natural time interval, when an excitation wave is provoked from the outside, provided that the point of stimulation is sufficiently far removed.* Thus in Fig. 20 *e* represents an external and *i* an internal contact, and the epicardium is stimulated 10 mm. away. The excitation wave appears at the internal contact first and at the external contact after the natural

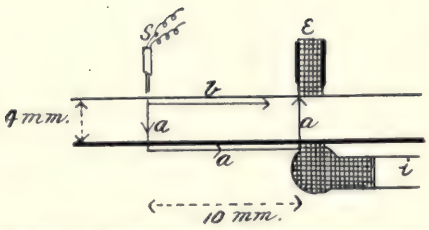


Fig. 20. Two contacts (e = external, i = internal) are placed on the epicardium and endocardium respectively, and the heart wall is stimulated at S, 10 mm. away. The excitation appears at the internal contact first and at a natural interval, before it appears at the external contact; it travels therefore by way of the Purkinje substance.

interval. It has travelled therefore along the path *a a a*, through 8 mm. of muscle and 10 mm. of the Purkinje system before it has travelled through 10 mm. of muscle (path *b*). Thus it prefers to pass through 10 mm. of Purkinje substance, rather than through 2 mm. or less of muscle.

The second experiment is similar in kind. Two contacts are placed on the right ventricle (Fig. 21) and the heart is stimulated at a point in the neighbourhood of the septum (n), some 10 or 15 mm. away. The interval between the arrival of the excitation process at p and d is relatively long. (The path taken is along c.) But if the point of stimulation is moved 30 to 40 mm. away (f) and the experiment is repeated, the interval is materially reduced; in a number of such experiments it is reduced *until it reaches the interval displayed by the natural heart beat.* In

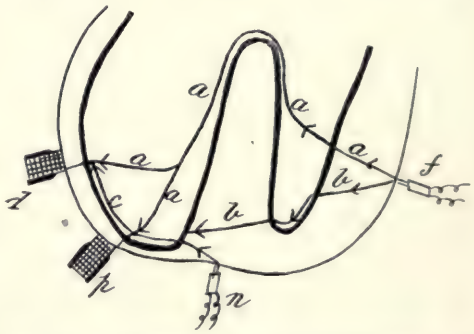


Fig. 21. A diagram of the ventricles, seen in vertical section. Two contacts, p and d, are placed on the right ventricle. The ventricle is stimulated at n and the excitation wave passes along the path c. The ventricle is stimulated at f and the excitation wave now appears at p and d at such times as to suggest that it travels through Purkinje tissue and bundle branches a, a, in preference to the shorter course b, b.

such instances the quicker though far longer path is over the septum and through the main divisions of the bundle (*a a* as opposed to *b b*). Let us sum up our findings. The spread of the excitation wave in the ventricle is controlled by the Purkinje system; it is hastened by the early branching of this system, especially in the left ventricle. The Purkinje system has a high rate of conduction as compared to ventricular muscle, and this quality also favours quick distribution.

Evidently, before we may end our search, we have to investigate the endocardial surface of the heart; this presents difficulties, but is in the course of completion. The excitation wave appears early inside the ventricle, and the time intervals appear to be very small between different endocardial regions. We believe that the earliest region of all is the upper part of the septum on the left side, and that other regions become active according to their distance from the main distributing tracts; but this has not been convincingly proved. Why then does the front of the right ventricle become active so long before superficial regions of the ventricle overlying the left papillary muscles? For a simple reason, namely, because the muscle is thinner. We have data of a very suggestive kind which appear to show that, as Purkinje conduction is extremely rapid, the excitation process starts almost simultaneously over the whole interior of both ventricles, and that the appearance of activity upon the superficies, while partially controlled by the distance from the main Purkinje strand, is chiefly controlled by the thickness of the muscle overlying the Purkinje substance. It is chiefly to this cause that we attribute the early appearance of the excitation wave over the front of the right ventricle, near its attachment, and at the vortex of the left

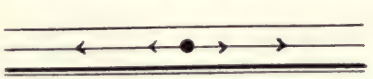


Fig. 22. A diagram illustrating the spread of the excitation wave in the auricle from a central node. The spread is along the muscle bands.

ventricle; for these are the thinnest points of the ventricular walls. According to our view the excitation spreads in the ventricle along the Purkinje system, and, appears on the surface by directly piercing the whole thickness of the wall (see Fig. 23); this piercing of the wall is aided by the penetration of the wall by isolated strands of the end arborisation of the Purkinje system.

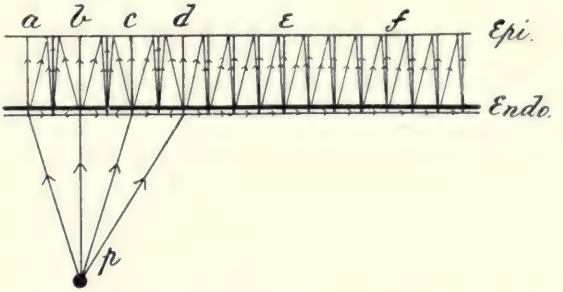


Fig. 23. The spread in the ventricle as it is conceived. The spread is from *p*, through branches of the Purkinje system; subsequently the spread is along the endocardial network and from this at right angles through the ventricular wall.

The observations which I have briefly surveyed will, I trust, take us far towards a final explanation of the normal electrocardiogram, for we are now in a position to state the regions which are excited when given deflections of the normal curve are inscribed; but this subject I shall defer. Our view of the distribution in the ventricle also helps us, so we believe, to understand the curious alterations of electrocardiograms met with in the hypertrophies; for a thickened left ventricle should delay the activity of the apical musculature, and by delaying penetration should deepen and prolong *S* in axial leads. However, this view is at present in the stage of tentative hypothesis.

Finally, a word on conduction rates in various regions of the heart. We find the conduction rate to increase as we pass from: —

1. Ventricular muscle to
2. Auricular muscle to
3. Purkinje substance.

It is to be remarked that the glycogen content of these tissues increases in the same order; but more important at present is the physiological significance of these variations in activity.

Distribution of the excitation wave in the auricle is expedited by the central position of the sino-auricular node and by a relatively high conduction rate, a relatively simple plan. The muscle of the ventricle conducts slowest because its function of distribution is a minor one; on the other hand, this, the driving chamber, is provided with a special system of distribution, clearly arranged to provoke almost simultaneous contraction; this special system is endowed with conduction powers of the highest order.

THE HERTER LECTURES

DELIVERED AT THE JOHNS HOPKINS HOSPITAL,
BALTIMORE, OCTOBER, 1914

"CLINICAL MEDICINE AND LABORATORY METHODS"

"The fourth is a Supinity, or neglect of Enquiry, even of matters whereof we doubt; rather believing than going to see."

"But the mortallest enemy unto Knowledge, and that which hath done the greatest execution upon truth, hath been a peremptory adhesion unto Authority; and more especially, the establishing of our belief upon the dictates of Antiquity."

"The testimonies of Antiquity, and such as pass oraculously amongst us, were not, if we consider them, always as exact, as to examine the Doctrine they delivered. For some, and those the acutest of them, have left many things of falsity; controllable, not only by critical and collective Reason, but common and Countrey observation."

SIR THOMAS BROWNE.

Chapter II

FIRST HERTER LECTURE

THE METHOD OF ELECTROCARDIOGRAPHY EXEMPLIFIED

Gentlemen,

When your Committee invited me to come to your Anniversary meeting and did me the honour of offering me this lectureship, it left me to choose the subjects of my discourses. The three lectures which are to be given have been arranged under the title of "Clinical Medicine and Laboratory Methods." The choice of this title seemed to me the most fitting for the occasion, for it allows me to present my subject matter in the form of a tribute to your School. Students of the Johns Hopkins University need no persuasion that an intimate association between the work of wards and laboratories is essential to-day. You have been leading advocates of this policy, your institutions are living monuments to enterprise of this kind. You have indeed the right to great pride that your University should have been the youngest in the van of those promoting the study of Medicine upon the exacting lines of the scientific laboratory. That you have been pioneers is a matter of common knowledge; that you retain your position is shown by your recent innovation in Medicine, which all European schools have closely watched with interest and lively expectancy. If you are in sympathy with the observations of my collaborators and myself, and I read your invitation in that sense, you are so, if I may presume to say so, because our work has been along lines which you have always approved and encouraged. There is

no closer bond of union between fellow-workers than the knowledge that the methods which they pursue are harmonious, that the trains of thought are of a kind. Laboratory methods as applied to the study of clinical medicine have come to stay; instruments and methods of precision are gradually relieving medicine of its past stigma; they are lifting it to the plane of its sister sciences, its true and proper status. We have been too content in the past with opinion, in the future we shall rest our case upon fact; our philosophy takes shape as it is moulded with additional and certain knowledge. To my colleagues in this field, I would say, our fight is not yet done, there lies before this generation a grand opportunity, a successful struggle for freedom. Let us go forward in a progressive spirit, casting from us the fatal traditions which dog our footsteps. The history of medicine is a history darkened by the dust of faith and superstition. Our abode is still unclean; the broom has yet to sweep the house again; let us retain it in our hands till its appointed task is done; there are many dusty corners, the cobwebs still cling thickly to the rafters.

Yours is a new country; young workers in older countries look to you to lead where they may follow; they see you leading where some day they aspire to follow. They send you this message, to continue to be their guide in the final emancipation of Medicine as Science.

I would awaken profound distrust of authoritative utterances, especial distrust of suggestive but unproved doctrines; our traditional teachings teem with them; let each statement receive support to the hilt, evidence is never too complete.

It has been my lot recently to examine some old established faiths in respect of cardiac hypertrophies. I do not propose to speak of them at the present time. The method has been similar to Müller's, accurate weighing of the separate heart chambers. What the result? Little beyond sweeping; the destruction of one's belief in the power to gauge preponderance

of this or that heart chamber by bedside tests; the conviction that mechanical factors are not the sole, nay, oftentimes not the chief agents at work; a clear appreciation that the whole subject must be reopened to new and more exacting investigation. It has also been my lot to join in investigating certain forms of breathlessness, and to this subject I propose to devote a later lecture. If you agree with the conclusions which I shall then draw, you will again see that it is urgently necessary for us to revise our ideas in respect of dyspnœa. So in many other directions our information is scanty or ill-founded; it is so because we have been content to listen to the voices of old times, because we have failed clearly to appreciate that workers of the past were fearfully crippled by lack of means to solve the problems with which they wrestled; because in our hearts we have refused to believe in Medicine as an exact science.

There is a field of clinical medicine in which progress has of recent years been considerable; so considerable that perhaps we are unable fully to grasp its significance at the present time. It is that which has refined our knowledge of movements of the heart chambers. If you took a clock to a mechanic for repairs and forbad him to remove its case, you could readily conceive his predicament; a similar problem is presented to each of us when confronted by a patient with heart disease. The mechanism of the heart, like the mechanism of the clock, has been veiled from view; listening to its sounds, we might gauge its pulse, as a child listens with wonder and bewilderment to the ticking of a watch, or eagerly scans the circulation of its hands.

Labouring under these conditions, an instrument of precision has been placed at our command, an instrument which permits us to record the inner workings and brings us into direct contact with its wheels. This instrument is the string galvanometer of Einthoven.

It is not possible in this lecture to cover the subject of electro-

cardiography; it is possible only to choose some few of the outstanding problems which have been elucidated largely by its aid. Those chosen have been chosen chiefly to illustrate method, and especially to confirm your conviction that clinical disorders may be imitated and studied in the laboratory. It is a common misconception that the study of irregularities of the heart's action ends with irregularity; that is far from being the case. It may be unhesitatingly stated that graphic methods are slowly but surely altering our whole conception of cardiac disease; the chapters which deal with cardiac syncope, palpitation, acute dilatation, heart strain, the diagnosis of myocardial disease, and cardiac failure are to be rewritten in the light of modern observations. But we owe them other and greater debts. Graphic work has dealt as severe a blow to the prestige of anatomical pathology as any it has received of late years. Not that I desire to deprecate this line of study; but clearly, as our prime business is with the living and not with the defunct organism, so the pathology of the wards must take precedence to that of the dead house. Graphic records are records of function, normal or pervert; it is of pervert function that our patients complain. Graphic work sharpens our perceptions, it provides facts which are intensely satisfactory as a basis for argument. The records are clear messages writ by the hand of disease, permanent and authentic documents which silence dogma.

The physiological electrocardiogram is as you know a direct record from the muscle of the heart, a record of the electrical changes associated with its beating. Inquire of this instrument the nature of the heart beat in a normal subject, it inscribes a hieroglyphic of the form which I now show you (Fig. 24). Our first task is to learn the meaning of this strange writing; our Rosetti stone is the heart of the lower animals. If we record the movements of the separate chambers of the

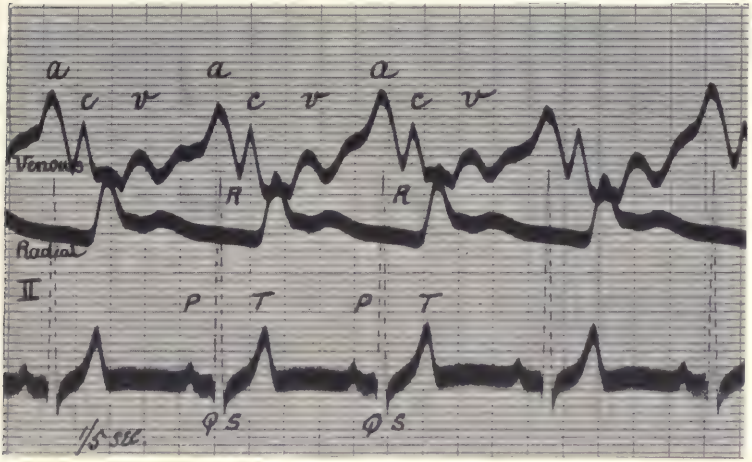


Fig. 24. Simultaneous venous, arterial and electrocardiographic curves, taken from a normal human subject. Illustrating the method of recording the movements of the several heart chambers. "*a*" in the venous curve, *P* in the electrocardiogram, represent the activity of the auricle. "*c*" and "*v*" in the venous curve, *Q*, *R*, *S* and *T* in the electric curve, represent systole of the ventricle.

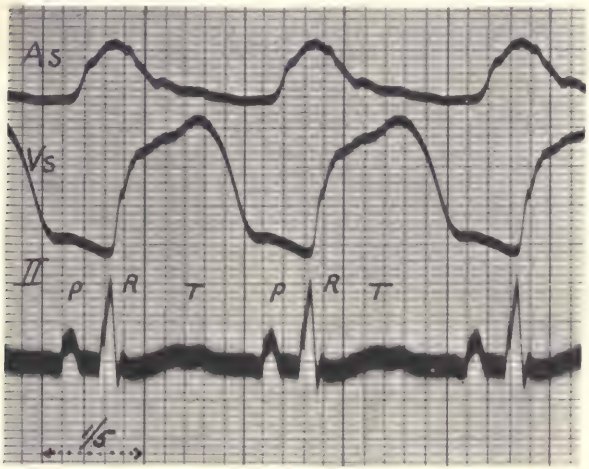


Fig. 25. An electrocardiogram from a dog with simultaneous curves from auricular and ventricular muscle; to show how the relations of electrocardiographic deflections to muscular events are studied.

dog's heart, and allow our galvanometer simultaneously to write its message (Fig. 25), we find it speaks of two events; it records the activity of the auricles and of the ventricles. The deflection *P* is the representative of auricular activity, though it slightly precedes the contraction; the deflections *R*, *S*, and *T* speak for the activity of the ventricles. The instrument not only signals these chief events, it tells us if the sequence of contraction in the muscle elements of a given chamber is normal. The normal curve *P* is given by a contraction coursing along normal auricular paths only; the usual deflections *R*, *S* and *T* by a beat following physiological paths in the ventricle only. Abnormal beats of either chamber are portrayed by curves of peculiar and distinctive forms. In a given case the type of curve is controlled by the direction of contraction in the muscle, relative to the position of the contacts upon the body; it is controlled therefore by the point at which the contraction originates. Let me illustrate these statements, which are the first grammatic rules of this new language.

In the first example which I show you are two curves; the one (Fig. 26) taken from a patient who exhibited a regular coupling of the pulse beats. The electrocardiographic curves show the same coupling, and each beat of a couple consists of an auricular portion *P* and of a ventricular portion, *R*, *S* and *T*. It is an example of an irregularity due to what are known as auricular extrasystoles. But if you examine the curve in detail, you see that the second beat of each couple, the premature one, resembles the first beat of each couple in every respect; first and second beats have followed the same muscle paths and the disturbance which gives rise to the second beat must have had its seat, if our rule holds true, in that portion of the heart from which the first or normal beat arose. That this is so is shown by the next curve (Fig. 27). It is an experimental replica of the first, and was produced by stimulating the heart at the seat of natural impulse formation. A duplicate could be pro-

duced in no other fashion. This is our method, to attempt to produce disturbances in the experimental heart, parallel to those which we see in the clinical heart. Our first clinical example is one in which we may locate a process of irritation in a given region of the right auricle, namely, in the immediate neighbourhood of the sino-auricular node, the structure which forms the natural pacemaker of the heart. My second illustration is

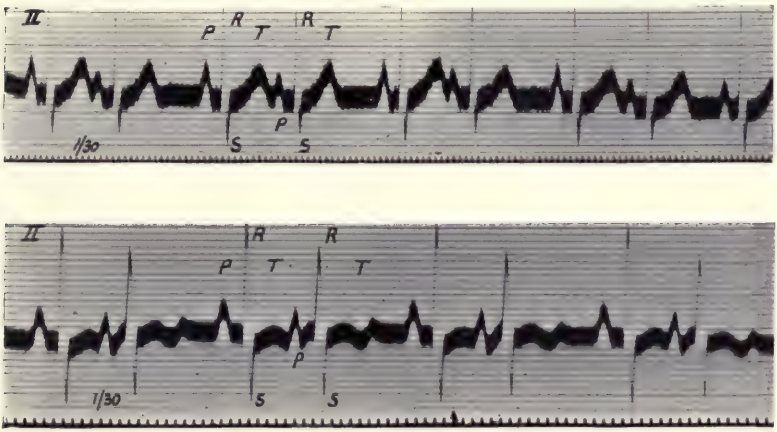


Fig. 26 and 27. Two curves showing coupled action of the heart beat, the first from a patient, the second from a dog. The coupled action in the experimental instance resulted from stimulation of the auricle in the region of the superior cava. To illustrate the method of investigating the origin of irregular heart action in clinical subjects.

similar (Fig. 28). Here is an electrocardiogram from a patient who exhibited an intermittence of the pulse and whose electrocardiograms not only portrayed numerous beats of normal outline but the curious atypical beats which give such large excursions. For comparison with this curve is one of experimental origin (Fig. 29) and the resemblance between the two is close. The experimental curve is written side by side with curves of mechanical shortening in auricle and ventricle, a script with which we are long familiar. The experimental irregularity was produced by stimulating the right ventricle.

The disturbance is confined to the ventricle as the mechanical records demonstrate, for the auricular rhythm throughout is undisturbed. The atypical beats which have arisen prematurely in the right ventricle, in virtue of their abnormal origin,

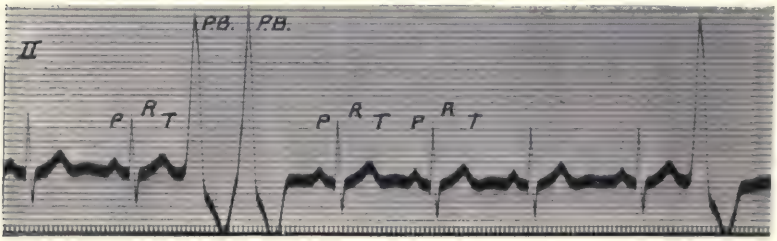


Fig. 28. A clinical curve showing an irregularity of the heart's action.

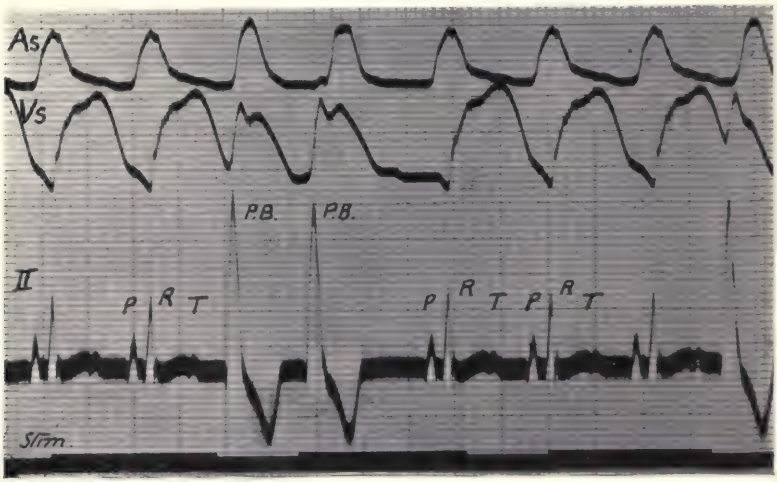


Fig. 29. A similar experimental electrocardiogram accompanied by curves of shortening of the auricular and ventricular muscle: the atypical beats were produced by stimulating the right ventricle.

have pursued an abnormal course through the muscle of the ventricle; it is to this that the changed character of the corresponding curves is due. It is in the manner illustrated that the seat of disordered heart action has been analysed.

I show you another clinical example of a curious change in the action of the heart. The first few beats of Fig. 30 are of normal type, the auricle and ventricle are beating in their usual sequence; but as the rhythm proceeds, its rate slows a little and suddenly the auricular summits disappear. We

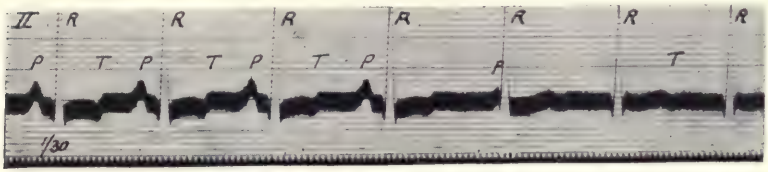


Fig. 30. A clinical curve showing escape of the *A-V* node as a result of slowing of the natural rhythm.

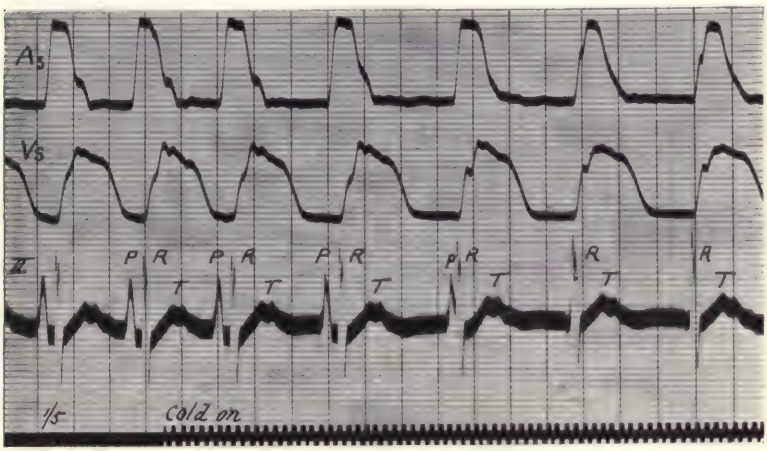


Fig. 31. An experimental curve showing similar slowing of the heart and escape of the *A-V* node when the sino-auricular node is depressed by cooling.

should possess no clue to the nature of this change had we no experimental data for comparison. The meaning of it is clearer when we study the companion curve (Fig. 31). Here we have electrocardiogram and mechanical curves, written simultaneously from the exposed heart of a dog. Normally the

heart beat starts in the region of the mouth of the superior cava in a structure termed the sino-auricular node (see Chapter I). If you depress the physiological activity of this structure by cooling, you obtain, as Ganter and Zahn have shown, a retardation of heart rate, and before long the auricular summits *P* are lost. They are lost, as the experimental curve shows clearly, because the contractions of auricle and ventricle are no longer in sequence but simultaneous, the auricular curve being buried and hidden in the ventricular curve. As the activity of the normal pacemaker becomes depressed by cooling, other centres become relatively more active, and the first in the race for control of the heart beat is the auriculo-ventricular node, which lies in the path between auricle and ventricle. When the upper node is cooled, the central node becomes the most active and dominates the heart's movements. Each time it produces a rhythmic impulse, this impulse travels to auricle and to ventricle simultaneously, the systoles of auricle and ventricle synchronise and yield this abnormal electrocardiogram.

I have spoken of the *A-V* node; it is the first part of a system of fibres which joins the auricles to the ventricles, the system as a whole serving as a channel of conduction for impulses passing from one chamber to the other. It is largely to work carried out in your institute by Erlanger and his collaborators that we owe our knowledge of the functions of this delicate strand of tissue, called the *A-V* bundle or bundle of His. The ventricle depends for its impulse to contract upon the auricle and upon the integrity of this tract. If the bundle is damaged by injury or disease, co-ordination between the two chief divisions of the heart is disturbed. I show you a series of curves which illustrate this disorder; a clinical curve (Fig. 32), and two experimental examples. Heart-block as it is termed may be produced in a variety of ways. It has been shown to follow when the bundle is pressed upon or crushed, by Erlanger and Hirschfelder, your experimentalists. It comes when the track

is damaged in any way, be this damage deliberate or be it through the accident of disease. It may be caused by the in-

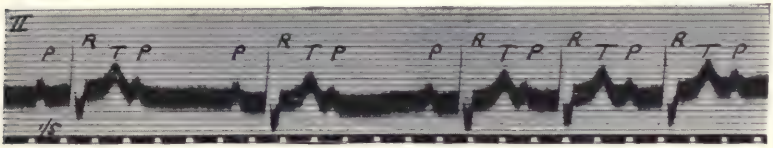


Fig. 32. A clinical instance of heart-block in a patient who suffered from chronic myocardial disease.

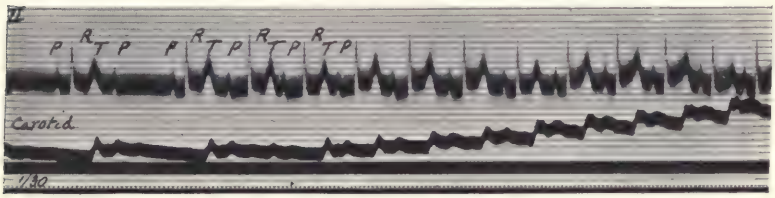


Fig. 33. The heart beat of a cat recovering from asphyxia. A period of 2:1 heart-block passes into the natural rhythm.

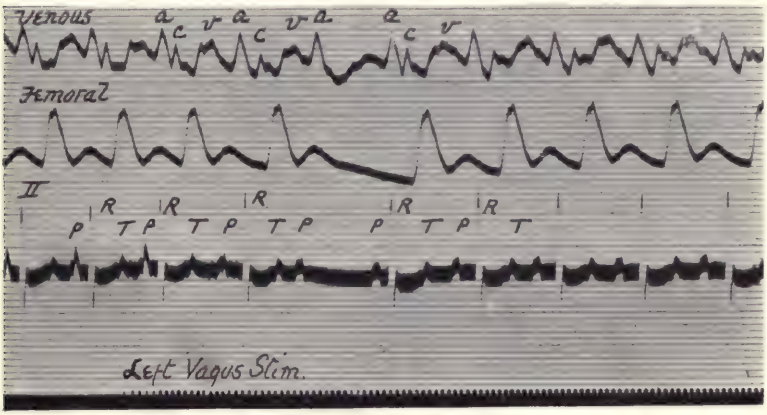


Fig. 34. Venous, arterial and electrocardiographic curves from a dog, showing heart-block as a result of stimulating the left vagus.

troduction of poisons into the circulation, such for example as diphtheria toxine, digitalis or the products of asphyxia (Fig. 33). It is produced by stimulation of the vagus, more espe-

cially the left nerve (Fig. 34). All these methods of producing block experimentally have clinical parallels. The most important are those in which definite lesions are to be found in the bundle region. The bulk of the ventricular muscle is silent in disease; affections of the bundle or its branches tell us often of an active or chronic process in the myocardium. As you know, heart-block is responsible for one of the major forms of cardiac syncope; where a slow pulse action is accompanied by attacks of loss of consciousness (Adams-Stokes Syndrome). It is experiment, and experiment only, which has taught us the clinical varieties of this condition.

We come to the most frequent and important disorder of the human heart beat, that so familiar to you as an accompaniment of failure of the muscle. The irregularity of the pulse which, on account of its complexity, has given rise to the term delirium cordis, was one of the last to receive adequate explanation; it has been studied since the active days of Marey, Sommerbrodt and Riegel. The first clue to its real meaning came from two laboratory workers in this land, Cushny and Edmunds; it is now definitely known to result from what is termed fibrillation of the auricles. That knowledge has been gained directly and exclusively from animal experiment, conducted side by side with clinical observations. Without such experiment we could have gathered no true conception of the events in the heart. This discovery has explained a multitude of obscure phenomena, it will continue, if I mistake not, to shed light upon the pathology of heart disease for many years to come. When the auricles pass into fibrillation they cease to beat and their walls, standing in a position of diastole, exhibit small flickering tremulous movements, which are the expression of inco-ordinate activity. Their function of propelling blood to the ventricles is lost; they no longer serve as reservoirs while the ventricle is contracted; the blood stagnates perpetually in them, the formation of muscle clots is promoted; heart murmurs become

altered; such activity as the auricle possesses is expressed in a malignant fashion, it lashes the ventricle to a quick and disordered movement, exposing any weakness of the ventricular muscle, if such exists, for the muscle cries out against the increased strain. The arterial blood pressure sinks, venous pressure rises; the onset of this condition is the most important contributory cause of cardiac failure of which we have real

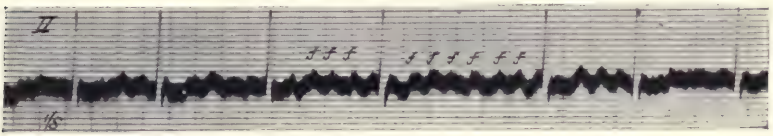


Fig. 35. A clinical curve from a case of mitral stenosis and muscle failure, illustrating fibrillation of the auricles.

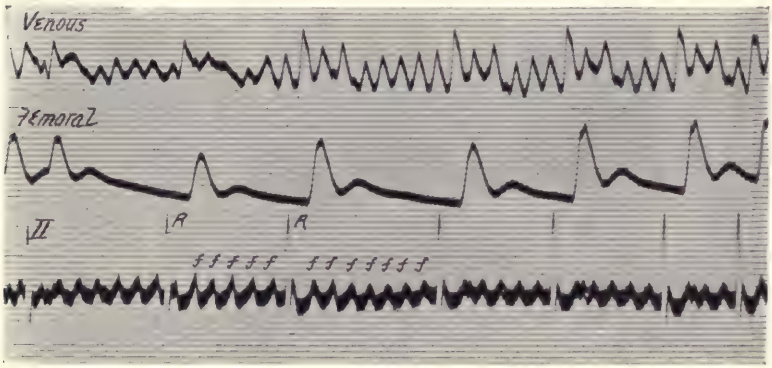


Fig. 36. Venous, arterial and electrocardiographic curves from a dog in which the auricles had been forced to fibrillate by faradisation.

knowledge. It was the electrocardiograph which first bore clear witness of its occurrence in the human subject. I show you two curves, clinical and experimental examples for comparison (Figs. 35 and 36). You will notice the irregularity of the ventricle in each, the absence of true auricular summits *P*, their replacement by the oscillations which characterise the condition. These oscillations are proved to arise in the auricle;

they represent the sum total of its delirious activity. The curves of fibrillation are of varied form, both in experiment and in human disease. Further examples are shown in Figs. 37 and 38. In Fig. 36 the auricular delirium was produced by faradisation of the auricles; Fig. 37 is a clinical curve; that of Fig. 38 resulted from the introduction of a poison into the

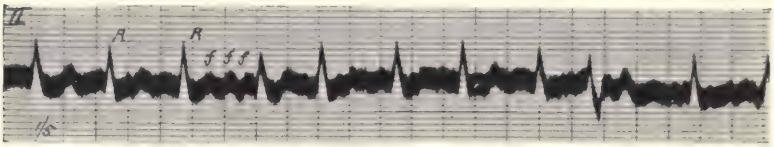


Fig. 37. Spontaneous fibrillation in the human subject in a case of rheumatic heart disease.

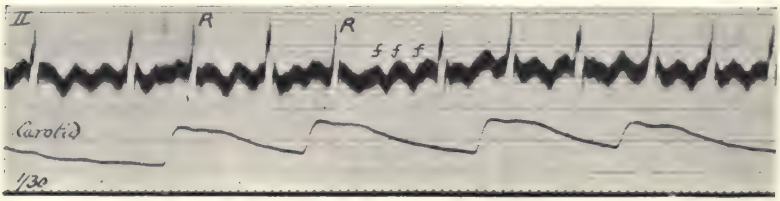


Fig. 38. Fibrillation of the auricles produced experimentally by the injection of glyoxyllic acid.

blood stream of an animal. We are still far from a full knowledge of the pathology in the human subject, but the first and important steps of isolating and recognising its true meaning have been taken finally. What its isolation means to us may be grasped when its prognostic significance is appreciated, and when its almost specific reaction to drugs of the digitalis group is realised. It is from the reaction of the heart, affected in this fashion, that digitalis owes its wide reputation; it is in these cases that it grips the heart and gives the slowing of pulse rate which relieves an exhausted muscle.

You will find clear instances of this affection described in Da Costa's historic treatise upon the irritable heart of soldiers; it has since passed on numerous occasions as an instance of heart

strain. You will see patients in whom, occurring as a temporary disorder, it promotes acute dilatation of the heart, and you will hear the term "dilatation" applied as the diagnosis in the case. It is but recently that we have appreciated that the fibrillation is the cause of the disturbance, and that the irregularity is not the sequel of distention of the heart. You will meet cases in which as a fleeting and recurring disorder it

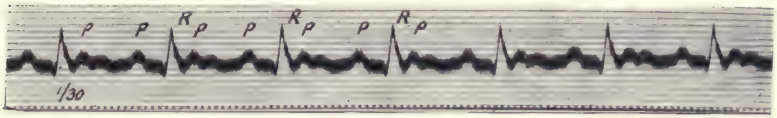


Fig. 39. Auricular flutter occurring in a clinical case.

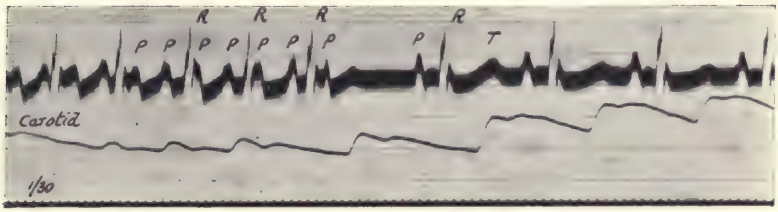


Fig. 40. The end of a period of flutter, produced in a dog by the injection of glyoxyllic acid into the blood stream.

promotes constant palpitation or even temporary loss of consciousness. You will meet it daily in your work as an associate and chief promoter of chronic heart failure. You will recognise it clinically because of this frequent association, because it is the only common irregularity which consorts with rapid heart action, because the ventricular beating is tumultuous and never constant from moment to moment. The ability to recognise it is a prime asset to-day in dealing with grave cardiac affections.

Our most recent acquisition is "auricular flutter" (Figs. 39 and 40). In elderly subjects a persistent and considerable acceleration of the heart's action may be found, but unlike the acceleration of fibrillation, this acceleration is associated as a general rule with regular action. In many of these patients,

galvanometric curves lay bare an unsuspected and astonishing fact. While the ventricle beats regularly at from 130 to 170, the auricular rate is precisely double. That the auricles may beat at rates of 300 or 350 per minute, and that such hyperactivity may be maintained for years, would have received no credence a few years since; it is now established. A clinical example of flutter, as it is termed, is to be seen in Fig.

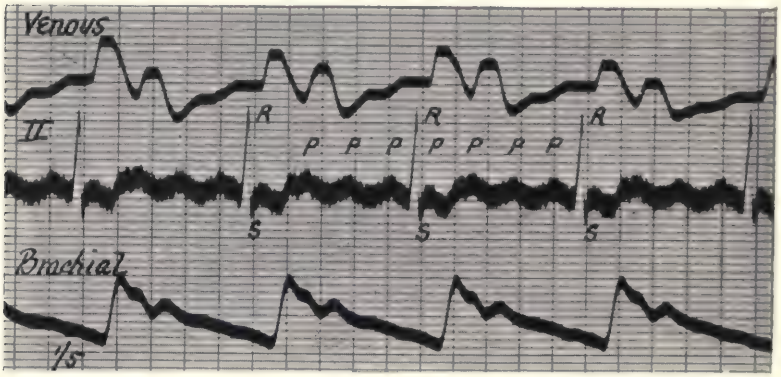


Fig. 41. Venous, arterial and electrocardiographic curves from a case of auricular flutter. The pulse beats regularly at 60, the jugular curve shows little or no sign of the auricular contractions. The electrocardiogram demonstrates a regular auricular rate of 240 per minute.

39, where the respective rates of auricle and ventricle are 228 and 114. The ventricle beats in response to each second auricular contraction; flutter generally exhibits this associated heart-block, the ventricles fail to respond to the highest auricular rate. It may be associated with higher grades of block, whereby the ventricular rate is reduced perhaps to normal limits and further concealed. The value of our laboratory method cannot be more clearly illustrated than by clinical cases of this type. On several occasions I have examined patients when the ventricle and pulse were beating regularly at perfectly normal rates, and in whom no suspicions of the auricular rate were awak-

ened until the heart was submitted to this electrocardiographic test. Fig. 41 is from a case of this kind; it discloses an unsuspected auricular rate of 240 per minute; the pulse rate is 60 per minute. Now these cases of auricular flutter, where there is extreme though regular acceleration of auricle, are not so infrequent as we at first supposed; the affection is a serious one, for even though the ventricular rate is but half the auricular, it is usually very fast and taxes an unhealthy or aged heart to the utmost; moreover, there is a constant risk in many such cases that the ventricle may respond to the faster rate and that an intolerable burden may thus be imposed upon it. It is a fortunate thing that we have a sure remedy for such patients; flutter has affinities with fibrillation, for digitalis will slow the ventricle and maintain its rate within bounds in flutter as in fibrillation; the drugs acts by increasing the pre-existing heart-block. I have seen no patient in whom this reaction could not be obtained, and in many, so I find, the reaction may be carried a step farther. If digitalis is pushed and is tolerated, the auricles pass from flutter to the higher grade of disorder, fibrillation. You might think the effect undesirable, in reality that is not the case. Flutter is essentially a persistent condition and untreated may be maintained during the rest of the patient's life. Change the mechanism by the exhibition of digitalis and the production of fibrillation, and, having accomplished this end, relax the drug; the heart returns, not to flutter, but to the normal rhythm. I well remember the first case in which this reaction was clearly demonstrated. It was in a French polisher admitted to hospital with a ventricular rate of 160; the auricles were beating at 320 per minute (Fig. 42*a*). Upon digitalis the pulse fell rapidly to 80, the auricular rate persisting as before (Fig. 42*b*). An increase of the dose now caused the onset of fibrillation (Fig. 42*c*), when the drug was withdrawn the normal rhythm was restored within a short time (Fig. 42*d*). The man was admitted with all the classical

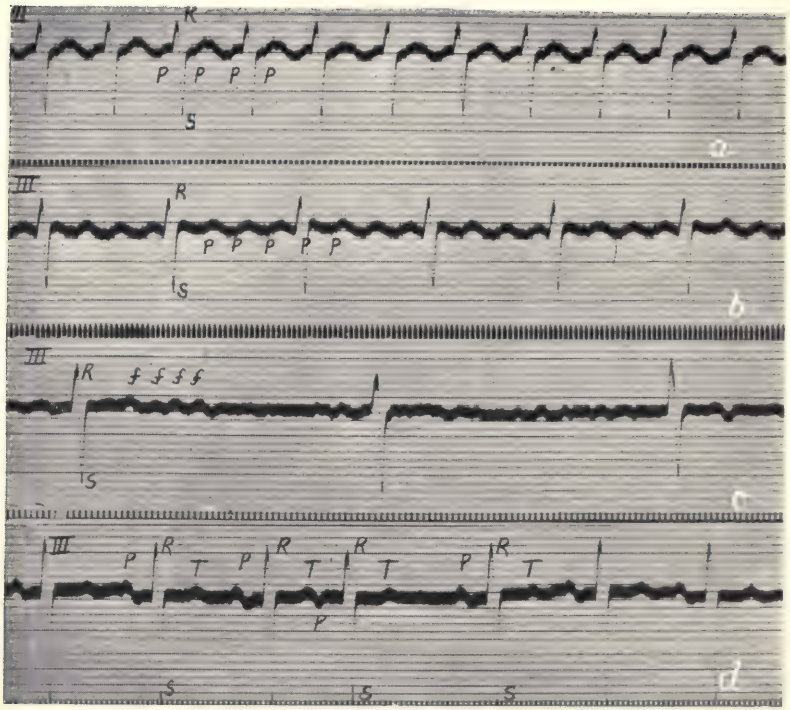


Fig. 42. *a*, *b*, *c* and *d*. Four curves from a patient who exhibited auricular flutter. (*a*) Before treatment; the auricular rate is 320, the ventricular 160 per minute. (*b*) While upon digitalis; the auricular rate is still 320; the ventricle beats at 80 per minute. (*c*) After pushing digitalis, the auricles fibrillate; eventually, after relaxing the drug the normal rhythm is restored (*d*).

signs of cardiac failure, he returned to work. Some few months later the flutter returned, but being treated once more in the same fashion, it was again abolished. That is three years since and our patient is still in comfortable health and fully engaged in his trade.

Chapter III

SECOND HERTER LECTURE

THE RELATION OF AURICULAR SYSTOLE TO HEART SOUNDS AND MURMURS

Gentlemen,

The subject with which I propose to deal to-day as my second illustration of the application of laboratory method to the clinical case is that of the graphic registration of heart sounds. And this subject has been selected from two points of view. First of all, because phonograms provide us with pictorial representations of auscultatory signs and have no inconsiderable value in this respect for teaching purposes. A few selected phonograms accompanied by accurate descriptions bring home to the student the nature of the signs which he observes, and impress the simpler lessons of acoustics in a facile and clear cut fashion. The sounds conveyed from chest by stethoscope to ear set in motion the tympanic membrane; they cause the recording instrument to vibrate in a similar fashion. There is however an important distinction between the impression gained from the writing on paper as we see it and those which come to us through the more direct channels of the auditory nerves. To those who are accustomed to inscribe these records and also to listen to the beating heart, having experience of its sounds, nothing is more impressive than the ability of the brain to discriminate; attention is concentrated for the moment upon sounds of one kind, perception of interfering sounds is meanwhile largely or wholly in abeyance. A delicate phonograph records all sound vibrations transmitted to it, be they of cardiac, respiratory or extrinsic origin; a short and

combined experience of recorder and stethoscope soon gives prominence to a fact which to a student, as he becomes clinician, rapidly recedes to the background; the living chest is filled with a babel of tongues, the sympathetic ear heeds one voice. So it happens, when we scan our first acoustic records, that their complexity bewilders us, and to analyse them we confine ourselves at first to the more simple documents, and especially to those which represent in a relatively pure form the sounds which we propose to study. But the lesson is not lost; our admiration for the delicacy of the auditory mechanism is a thousandfold enhanced, and we learn that in the discrimination of pitch, tone and intensity, the physiological ear has no rival. These remarks bring me to the statement of my second object. It is to show that although the ear has this unquestioned superiority, and that although the auscultatory signs of heart disease have been minutely studied by its means and by countless workers, we have yet much to learn and much which can be learned only by the employment of mechanical aids. The chief value of the recorded heart sound is the possibility of accurately timing its occurrence in relation to the events of the cardiac cycle.

It is not my purpose to consider the history of sound records, neither shall I attempt to cover a hundredth part of the whole field of fact and speculation surrounding heart sounds and murmurs; but I shall be content to describe in simple terms a single device, and to pass to brief descriptions of some recent observations which seem to show how important the influence of the auricular pressure upon sounds and murmurs may be.

In the first figure (Fig. 43) a tuning fork is represented as emitting sound; with each movement of the fork towards the right, the air in this direction becomes compressed; the tension is relieved in every direction, amongst others towards the recording instrument; it travels through the atmosphere, fading as it travels, as does a ripple on the surface of water; as the fork returns from its swing, the same neighbouring air becomes

rarefied and this rarefaction follows the wake of the condensation and is transmitted through space. At a given moment, therefore, the air surrounding the fork is arranged in alternate layers of condensation (*Co*) and rarefaction (*Ra*); each and all

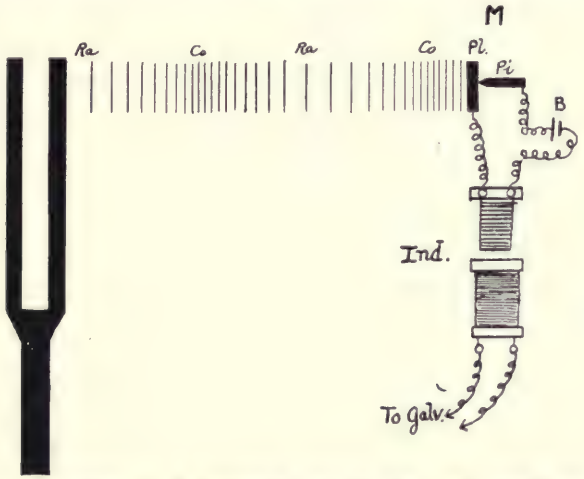


Fig. 43. A diagram of a vibrating tuning fork, the sound oscillations from which are recorded by a microphone (*M*). The microphone consists of carbon plate (*Pl.*) and point (*Pi.*) and these are in circuit with a battery (*B*) and the primary coil of an inductorium. The secondary coil is directly connected to the string galvanometer.

are travelling along radiating lines. Our recorder contains a thin carbon plate (*Pl*), which being sensitive to movement, oscillates in synchronism with the condensations and rarefactions as they arrive; it is the oscillation of this plate which yields the record, as it is the similar oscillations of the tympanic membrane which convey the auditory impression of sound; for the alternate layers in the air form the sound vibrations. The movements of the plate are traced by allowing it to rest against a carbon point (*Pi*) and by recording the changes in resistance which occur between the two carbon surfaces as the pressures between them vary. For this purpose a constant current is transmitted from carbon to carbon and in the same cir-

cuit a primary coil is placed. The resistance between carbon and carbon varies as succeeding phases of the sound vibrations reach it, and so the current flowing through the circuit varies; the changes in the current are magnified by the secondary coil and pass into the sensitive string galvanometer. So each movement of the fork is accompanied by a movement of the string and our record is in reality a record of the fork's oscillations. Similarly in taking tracings from the chest wall, the sounds are records of the valve vibrations transmitted through the chest wall and stethoscope to the carbon plates, which form the microphone, and thence to the galvanometer.

Fig. 44 is a record of the movements of a tuning fork, or if you will the sound it yields, beating regularly at 50 per second. You see that the vibrations are regularly placed, and it is to this regular arrangement that the sound emitted owes its musical quality. As you know, the pitch is regulated by the frequence. Comparable records are to be obtained from vibrating strings and from time to time the sharp edge of a broken valve. The loud and musical murmurs which are not infrequent after rupture of the aortic valves are produced in this manner; examples are seen in Figs. 45 and 46.

Accurate timing of sounds is best accomplished by the simultaneous record of sound and electrocardiogram. The records in the accompanying figure were taken for the most part with separate galvanometers placed side by side; in all instances the records are so arranged that points of the two curves lying on the same vertical line represent the same time instant. The onsets of first and second sounds and their relation to systole in auricle or ventricle may be estimated by a comparison of the curves, allowing a short interval in the electrocardiogram for the appearance of the excitation wave before the contraction wave. But so far as the ventricle is concerned, the most exact method in a given case is to take the onset of the recorded first and second sounds, where they are unquestionable, as the

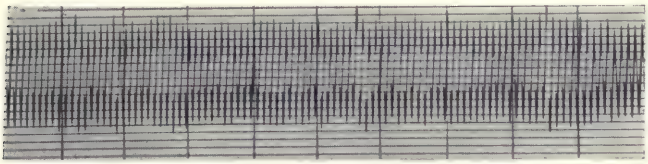


Fig. 44. A tuning fork record.

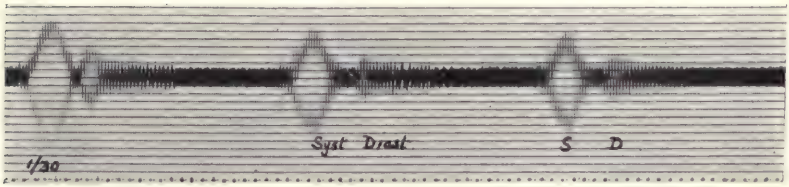


Fig. 45. Musical to and fro murmur at the aortic cartilage.

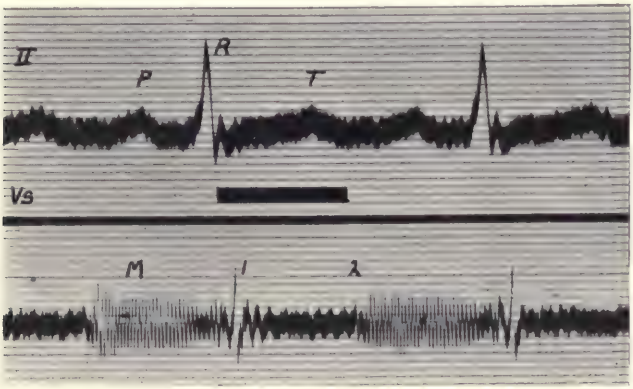


Fig. 46. A diastolic murmur of aortic origin and musical quality.

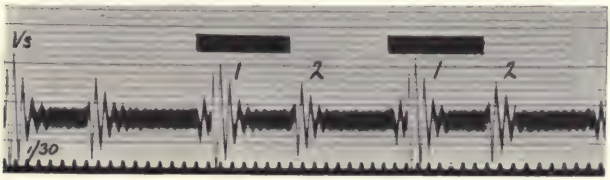


Fig. 47. Record of normal apical heart sounds.

indices of onset and offset of systole. It may be necessary when the record is complicated by murmurs to take a control record from the same case, with the object of obtaining the 1st and 2nd sound in a more uncomplicated form from a neighbouring point upon the chest wall, and then by comparing the two plates, the necessary data are obtained.

The relation of the onset of the 1st and 2nd sounds to the electrocardiographic deflections is subject to some variation. The 1st sound begins from .002 to .026 seconds after the commencement of *R*, or from .011 to .039 seconds after the commencement of *Q*, when this deflection is present. The 2nd sound may start .035 seconds before, or as late as .028 seconds after the end of *T*; as a rule it begins within a very short distance of the end of *T*. As a general standard we may use *R* and take a point 1-50th of a second after this upstroke; it will represent the onset of systole with no greater error than 1-50th of a second. Similarly, we may take the end of *T* as representing the offset of systole and the error will be no greater than 1-30th of a second.

Generally speaking the natural heart sounds are complex; the oscillations are irregular in time and amplitude, varying much from subject to subject. A relatively simple record from a normal heart is seen in Fig. 47; you will notice that the 1st sound begins as a crescendo, rapidly reaches its maximum and tails away as a diminuendo. The 2nd sound, as is usual, is abrupt in its onset, consisting as a whole of a simple diminuendo. In the instance of the musical murmurs which I have shown you, the number of vibrations was 138 to 180 per second. The number for the natural 1st sound is much less, being 45 to 70 per second, and for the 2nd sound, 40 to 86 per second. This speaks for the valvular origin of both sounds in the main, for the frequence depends upon the length and mass of the vibrating structure and upon its state of tension. Incidentally we may compare these sound records with records of the spoken

syllables *lub-dup* (Fig. 48); and a comparison of this kind at once demonstrates how imperfect is this phonetic representation. Both *lub* and *dup* are in reality each built up by at least

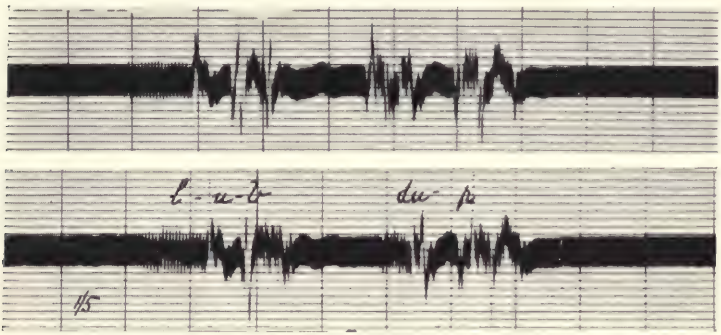


Fig. 48. Two records of the spoken syllables "*lub-dup*."

three distinct vocal acts, though in rapid speaking there is some slurring.

We pass to our main topic, the influence of the auricles upon heart sounds. That auricular contractions may give rise to audible sounds has been suspected for a long while, that such is indeed the case was shown after dissociation of the contractions in auricle and ventricle was discovered. It is now well known that in cases where the ventricle is beating slowly in response to its own inherent rhythm and where the auricular rate is still normal and therefore much faster than the ventricular, the long diastoles of the ventricle may not be silent; but that faint thuds may be heard at apex, epigastrium or heart base, which can only be attributed to contractions of the auricles. This explanation is clearly justified by such curves as that of Fig. 49; here the auricles are contracting at three times the rate of the ventricles as the simultaneous electrocardiogram demonstrates. In every diastole the auricles beat twice and on each occasion produce a faint and double sound. The first element of this double sound does not begin immediately with

auricular systole, but when the latter is well advanced; its cause is not clear; that it is not due to the passage of blood to ventricle seems evident, for a similar sound occurs during the end of ventricular systole where another auricular contraction falls. Possibly it is due to the actual contraction of the muscle of the auricle and to tension in its walls. The second element is I think attributable to the cessation of flow from auricle to ventricle and to consequent closure of the auriculo-ventricular valves, as Henderson has suggested; for this second element falls in early auricular diastole. When a stream of water is poured through an auric-

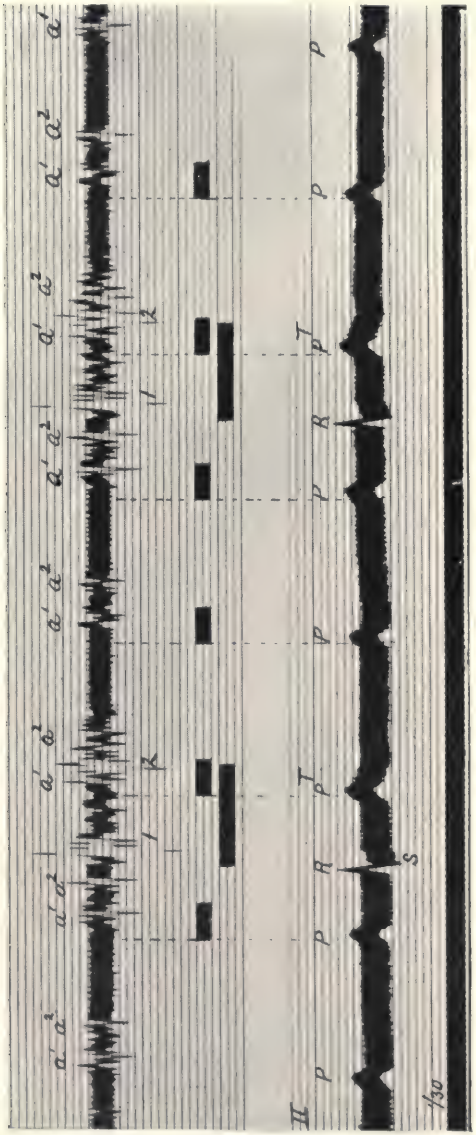


Fig. 49. A record of auricular sounds in a case of complete heart-block.

ulo-ventricular orifice, and this jet is abruptly broken, the valves immediately close. The sound is more intense when the auricular systole falls in early rather than in late ventricular diastole, and this is to be expected, for at such a time the ventricle is full and any opening of the valves must be followed by a quick return to the closed position. In heart-block, as a rule, the auricular contraction is followed by a single sound, and it is probably brought about in the manner to which reference has just been made. But if the auricular sound is audible in heart-block, why is it not in the normal heart beat? I suggest because the auricular and ventricular systoles are too near together. Normally the end of auricular systole is terminated sharply by ventricular systole. There is no intersystolic period. The swing of the A-V valves which is to be expected at the cessation of auricular contraction would coincide with closure and tension of these valves as a result of ventricular systole. Assuming this view to be correct, then if for any reason the closure of the A-V valves as a result of ventricular systole were delayed, we should expect double closure of the valves; the first resulting from the wake of the auricular systolic blood; and after a short pause a second closure resulting from ventricular systole. It is actually the experience that when the *As-Vs* interval is prolonged, a double sound is often audible, for it is in these cases *a fortiori* that gallop rhythm appears. It is also frequently present in those curious cases in which the excitation wave appears to take an abnormal course through the ventricular walls. Gallop or canter rhythm is of two kinds; in the commonest type the additional sound happens immediately before the natural 1st heart sound; in the second type, the additional sound lies in early or mid-diastole. A beautiful example of the first variety is seen in Fig. 50. That the first element of the canter lies in presystole is quite clear in this record; it is equally clear that it lies toward the termination of auricular systole, the *As-Vs* interval being a little pro-

longed. If we examine this curve in detail and focus our attention upon the composite sound, what strikes us most is the similarity of its two elements. The likeness is so perfect as to convince us that both elements have a common origin; the 2nd

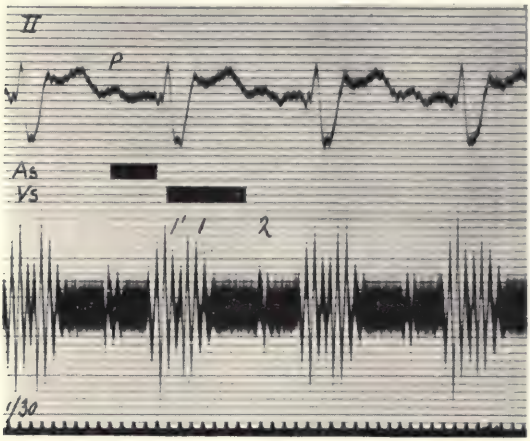


Fig. 50. Canter rhythm at the apex beat; from a patient who presented evidence of a right bundle branch defect.

element must be attributed to ventricular systole. The 1st cannot be so explained, for it begins outside the bounds of systole; but both elements may be assigned to closure of the A-V valves, the first produced by the termination of auricular, the second by the onset of ventricular, systole, in the manner already indicated. It is also to be remarked that in no instance as yet has a reduplication of this kind been seen where the auricles are in the state of inactivity associated with fibrillation; it has always been associated with a natural sequence of contractions, but as a rule with a sequence somewhat delayed by the interposition of an intersystolic interval. Examples in which there is no delay in sequence are to be seen in Figs. 51 and 52. In these the additional sound falls with the beginning or height of auricular contraction and is perhaps com-

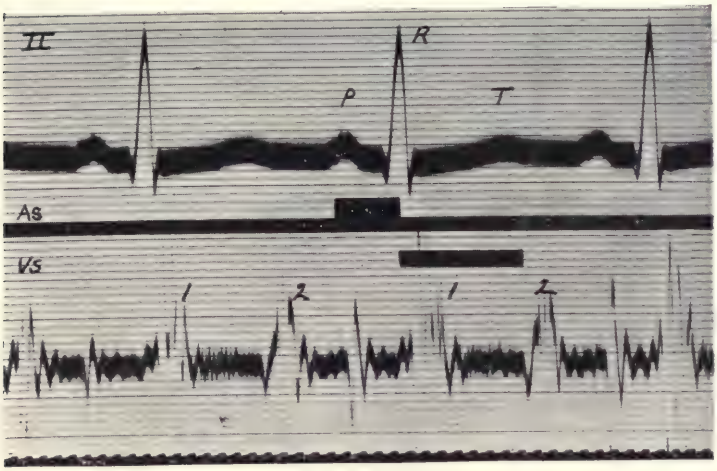


Fig. 51.

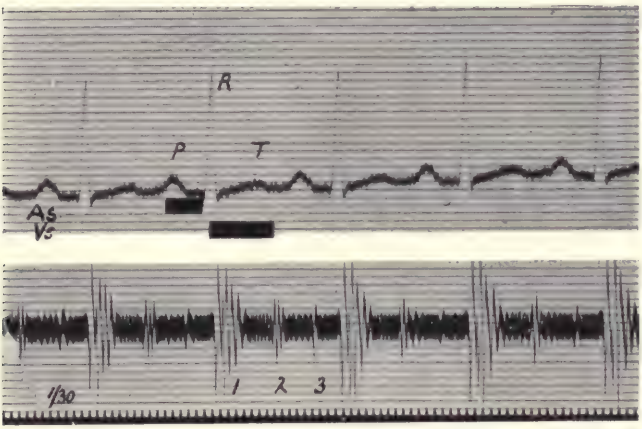


Fig. 52.

parable to the 1st auricular element of Fig. 49. It may be that in such cases we have to deal with hypertrophy of the auricle. In Fig. 53 the extra sound is in mid-diastole and here the height of auricular contraction falls immediately after and upon the end of the preceding ventricular systole; in all

probability, the sound has been produced, or at the least has been enhanced, by the auricular contraction.

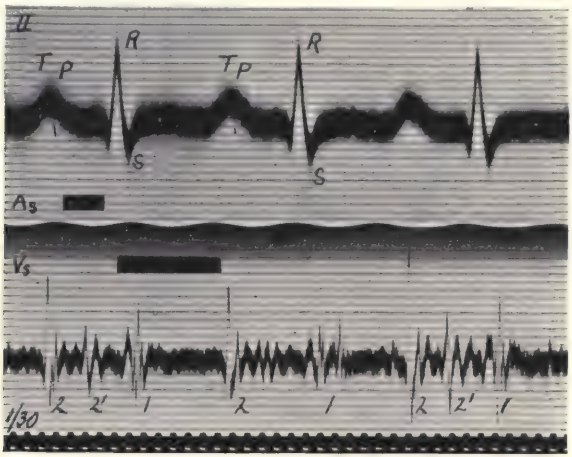


Fig. 53.

Fig. 51, 52, and 53. Examples of canter rhythm; the extra sound accompanying auricular contraction.

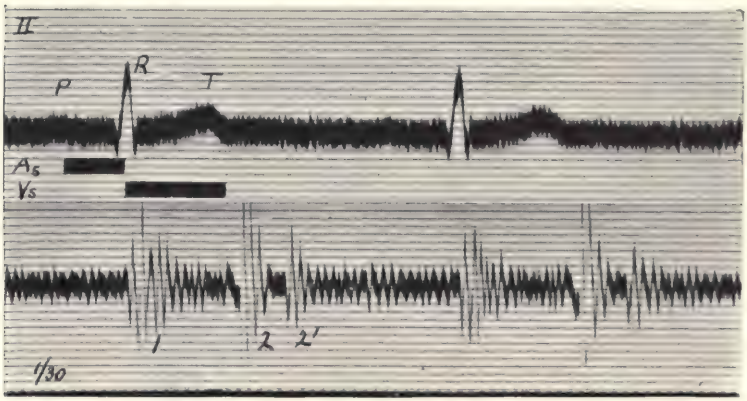
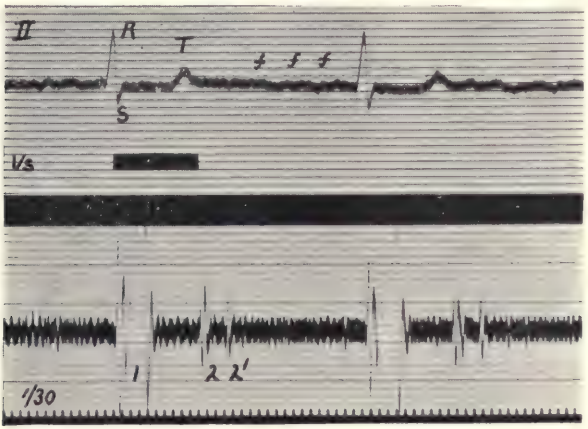


Fig. 54. Canter rhythm; the extra sound falling in early diastole.

What appears to be wide reduplication of the second sound is seen in Fig. 54; here diastole is long and there is no ques-

tion of auricular systole taking part, for the sound is far removed from it. Similar apparent reduplications are seen in Figs. 55 and 56, in both of which the auricles are fibrillating.



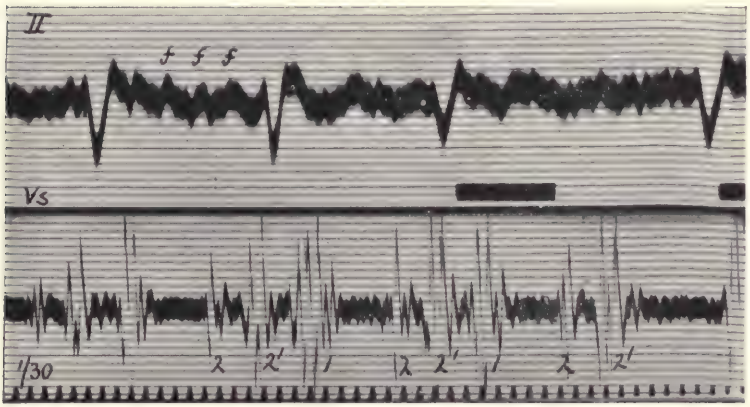


Fig. 55 and 56. Canter rhythms in cases of auricular fibrillation; the extra sound being related to early diastolic events.

This type of canter rhythm is very evidently of different origin to the first. It is not to be ascribed to asynchronous closure of the semilunar valves, for in all the figured instances the sounds

were of maximal intensity near the apex or the canter was confined to this region; and also because the elements stand too far apart from each other. In simple reduplication which may be ascribed to asynchronous semilunar closure, the two elements are fused and are scarcely distinguishable in records. The 3rd sound (the 2nd element of the reduplication) is due to some event occurring a little while after the *A-V* valves open in early diastole; it may be that these valves are set in vibration by quick filling of the ventricle and their consequent closure, in given cases, as Thayer and Hirschfelder have suggested in describing the third sound of the normal heart beat. Many of the instances which I show you are almost certainly exaggerations of this extra sound which may be heard in healthy subjects.

I leave the question of canter rhythm, fully aware that the description is incomplete, but content if I have satisfied you that, in some instances at all events, auricular contraction may be responsible for it and that we have still much to learn by careful study and the use of the graphic method.

Some little while since a curious change in the heart sounds was described by Dr. Griffith of Manchester in cases of complete heart-block. It transpires not only that the auricular sounds are audible in this disorder of the heart beat, but that the incidence of auricular contractions profoundly affects the quality and amplitude of the ventricular sounds. The variation is such that it forms a most valuable bedside test of complete heart-block when instrumental aids are not available. As Griffith described it, it consists of a great increase in the loudness of the 1st heart sound when an auricular contraction falls synchronously with the beginning of ventricular systole. The phenomenon is clearly to be seen in Fig. 57 and you will notice that the intensification comes when the auricular contraction slightly precedes the ventricular; if the relationship is reversed, as in the first cycle of this figure, the 1st sound

tends to reduplicate. A gradual change of intensity as the auricular systole gradually moves over the commencement of ventricular systole is seen in Fig. 58. All these 1st sounds are greatly accentuated but that of the first cycle especially so. The figure should be compared with Fig. 49 which is from the same case and taken at the same sitting. The complete physical sign, as you may hear it in almost any case of total dissocia-

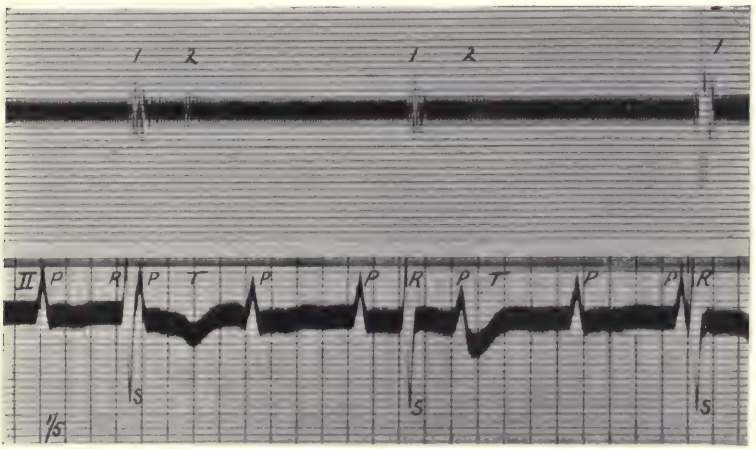


Fig. 57. From a case of complete heart-block; showing the accentuation of the 1st sound when the auricular systole overlaps the ventricular.

tion, when the pulse is regular, consists of an accentuated 1st heart sound occurring in a periodic fashion and associated also with periodic reduplication of both 1st and 2nd sounds. Such variation of the sounds is very striking; it occurs so far as I am aware in no other condition, being distinctive of *A-V* dissociation.

Mitral stenosis.

For the remaining time I propose to discuss the murmurs of mitral stenosis and their relation to events in the auricle. Let us consider in the first instance the characteristic murmur of mitral stenosis which accompanies a regular heart action.

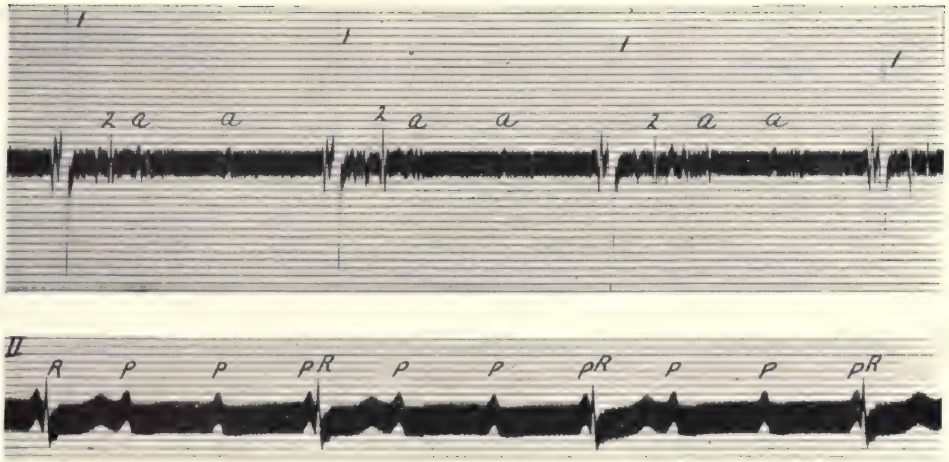


Fig. 58. From the same case as Fig. 49, showing four accentuated 1st sounds, gradually diminishing in intensity as the relation of *As* to *Vs* gradually alters. The records of the auricular sounds are also visible.

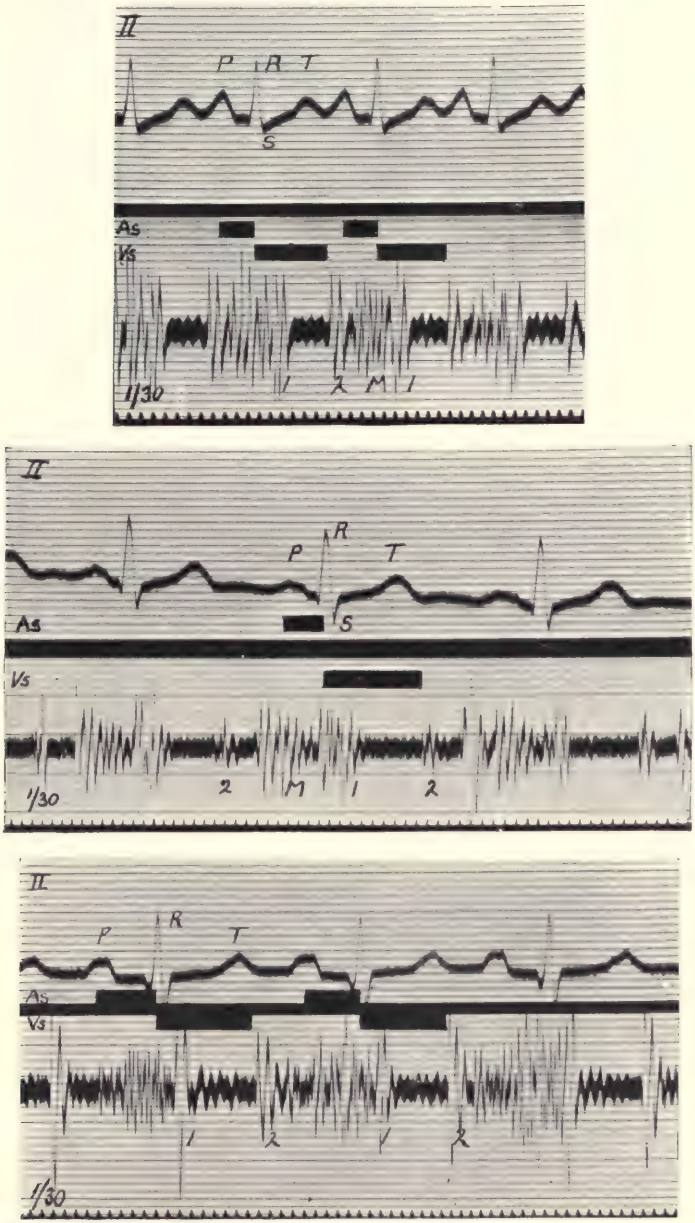
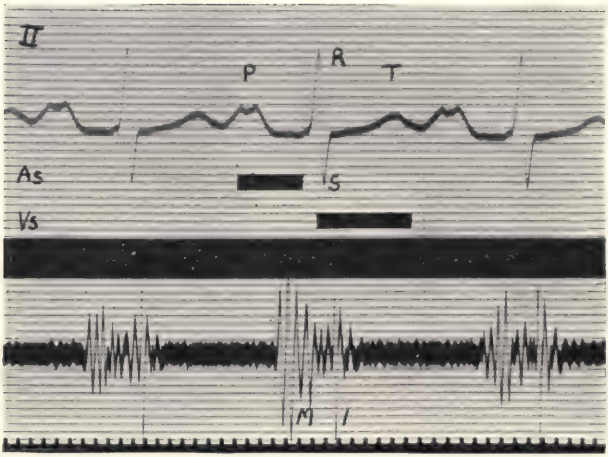


Fig. 59, 60, and 61. Examples of apical murmurs in three cases of mitral stenosis.

Called presystolic by almost universal custom, it is generally believed to be presystolic in time; yet as you are aware its actual position in the cardiac cycle has been hotly contested on many occasions. Ormerod, Barclay, Dickinson, and lastly Brockbank have held it to be in reality systolic. The final proof of its presystolic position has been supplied by graphic records. Even when it has a duration of no more than 1-20th or 1-30th of a second, it comes before the beginning of the 1st sound. Gairdner called it the auriculo-systolic murmur, and his suggestion that it results from auricular systole is almost certainly correct in the main; though this statement requires some amplification. In most cases of considerable stenosis where the heart's action is regular, for example in such cases as come to us in an out-patient department, the murmur usually occupies the whole diastole. This filling of diastole is due to the fact that there is generally some acceleration of the heart and the diastole is therefore short. Many murmurs commonly called presystolic in reality occupy the whole of diastole as graphic records show quite clearly (Fig. 59). They lie in presystole, it is true, but also in mid- and early diastole. The term presystolic murmur properly speaking should be confined to a murmur isolated in presystole. On listening to heart sounds at the apex beat, we are too apt to time murmurs relative to the 1st sound and to neglect the relation to the 2nd heart sound. I think too that a murmur is often called presystolic, not because it is so timed, but because it has the rasping and rumbling qualities which are usually borne by such murmurs. Timing by auscultation is often a difficult or impossible task if it is to be carried out with any pretension to accuracy. At all events the fact remains that isolated presystolic murmurs are comparatively rare; they occur when the heart rate is slow or when the stenosis is not extreme; an example is to be seen in Fig. 62. Two murmurs of the same quality may be present, the one in early and the other in late diastole; this condition is seen when

the heart rate is slow and the stenosis considerable. Thus the murmurs which accompany mitral stenosis in different patients are very variable in their time relations; they also vary greatly from cycle to cycle in the same patient and vary both in time and quality. The meaning of such variations will be discovered in the sequel. The murmurs of mitral stenosis have the lowest vibration frequence of any. The frequence, as a rule, is the same, it may be a little faster, as the vibration frequence of the 1st sound in the same case. The similarity of frequence speaks for the origin of the murmur in vibration of the mitral valve.

If we consider the simplest type of murmur, that which falls in presystole, we observe that it is related to auricular systole; the murmur commences near the height of auricular contraction (Fig. 62) or starting earlier is reinforced at this time (Fig. 60, 3rd cycle, and Fig. 61). Such at any rate are the common events. No one will doubt I think that the murmurs of mitral stenosis are produced by the passage of blood from auricle to ventricle through a constricted orifice. The relations of the simpler murmurs suggest that the propulsion of blood by auricular contraction is an important factor in their production. In some cases it is an all important factor and in these we may correctly call the murmur, as Gairdner did, auriculo-systolic. Figs. 62 and 63 were taken from a single case at a few days interval. In the first curve the murmur begins at the height of auricular systole, and lies wholly in presystole. This curve was taken from a case susceptible to the influence of digitalis and by administering this drug it was possible to alter the relation of auricular and ventricular systole. The influence of auricular systole upon the murmurs could be studied therefore in an exact manner. After the administration of digitalis the auricular systole lay, not in presystole, but in late ventricular systole and early diastole (Fig. 63). As an association the murmur altered its position, leaving presystole and appearing



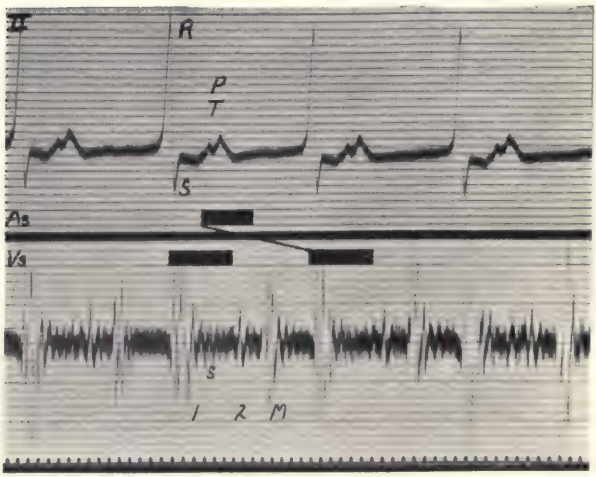


Fig. 62 and 63. Two records from the apex beat in a case of mitral stenosis, before and after the onset of partial heart-block.

in early diastole; as a matter of fact not in earliest diastole, but at a point in the cycle a little after the opening of the *A-V* valves.* The influence of auricular systole upon the murmur in this case can hardly be questioned. The appearance of a gap between murmur and 1st sound when the *As-Vs* interval is prolonged was first reported by Galabin; it has been emphasised from sounder data by Mackenzie in recent years. I would remind you too that Dr. Cohn of New York has reported an instance of mitral stenosis in which 2:1 heart-block developed as a result of digitalis administration and that when the block appeared and the auricle was beating at twice the ventricular rate, two similar murmurs were audible in each diastole, one in mid- and the other in late diastole. I have witnessed the same phenomenon on several occasions and have felt the double thrill at the apex in diastole. The importance of the auricular systole in influencing these murmurs is therefore beyond doubt.

Some years ago an extremely important observation was made by Mackenzie; if you examine the earlier papers of Galabin and Fagge, you will find it foreshadowed; for these authors noted the disappearance of the murmur of mitral stenosis when the heart becomes irregular, or its isolation in early diastole when the auricular contraction could no longer be recorded. But it is to Mackenzie's exact work that we really owe our chief knowledge of the behaviour of murmurs when the heart beat becomes disordered. He has spoken in the most decided manner upon the subject, and has stated that when irregularity of the ventricle,† which we now know to be attributable to fibrillation of the auricle, becomes established in a case of mitral stenosis, the presystolic murmur vanishes, and its disappearance he attributed to inactivity of the auricles during diastole. That Mack-

* In using the word "opening" one refers, in a case of mitral stenosis, to the time of the first entry of blood from auricle to ventricle.

† Ascribed by Mackenzie to "Nodal rhythm."

enzie's statement is in the main a correct one, graphic records proclaim. I may briefly describe the events as they are known to us. The murmurs of mitral stenosis, when the auricles are fibrillating, are peculiar; an *isolated* presystolic murmur is not heard; the whole diastole may be filled by murmur (Fig. 64),

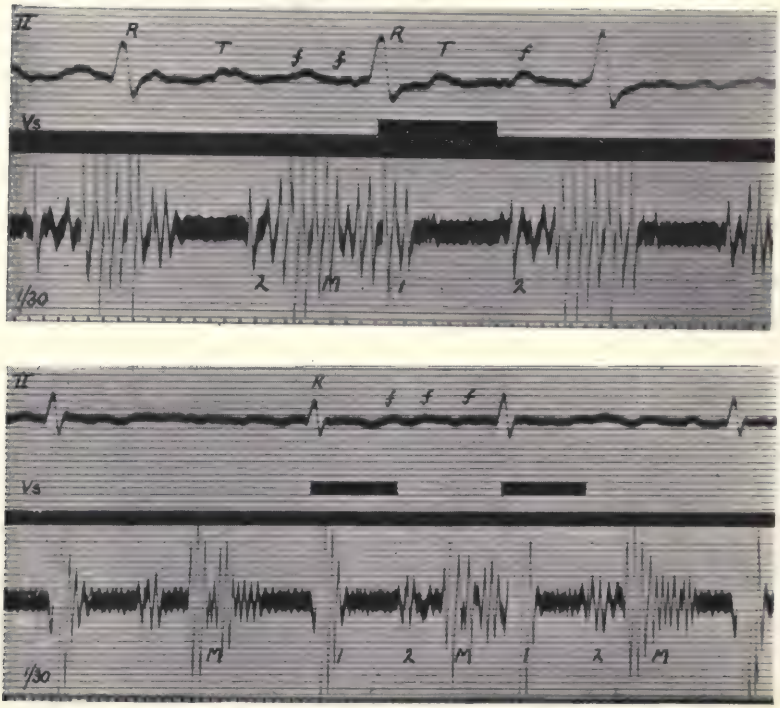


Fig. 64 and 65. Two apical records from a single case of mitral stenosis and auricular fibrillation, before and after treatment with digitalis.

and this occurs when the heart's rate is rapid and the stenosis is great, or if the rate is slower the murmur is confined to early diastole. The commonest condition is one in which short and long diastoles are mixed; and in which the former are filled by murmurs, while in the longer ones the murmur tails away and vanishes in mid- or late diastole (Figs. 65 and 66).

The important point to notice is that the fixed relation is to the 2nd and not to the 1st heart sound. When a case of mitral stenosis with fibrillation is first examined, the murmur generally completely fills the whole diastole (Figs. 64 and 67), or only

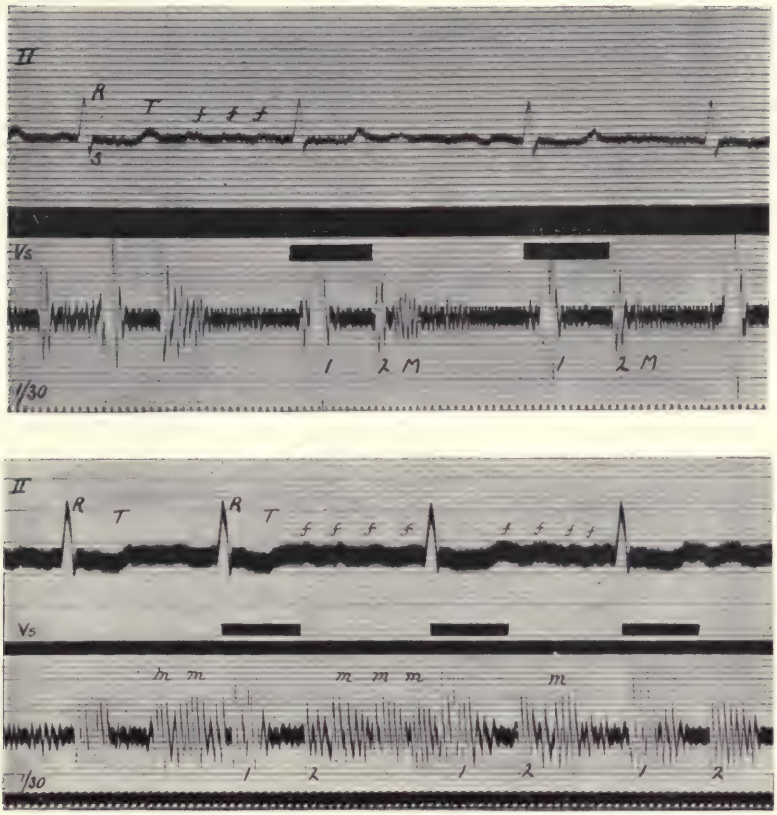


Fig. 66 and 67. Two apical records from cases of mitral stenosis with auricular fibrillation. In Fig. 67, the diastolic murmur shows notable sub-divisions.

fails to fill a very occasional diastole. As the heart slows upon digitalis (Fig. 65) the murmur persists but now tails away as diastole proceeds. A gap appears between it and the next 1st sound, and the length of this gap depends upon the length of the

particular diastole. The difficulty in properly timing the murmur lies in this variability; in reality the murmur is constantly early diastolic, but in some cycles it is curtailed by the quickly succeeding systole of the ventricle; in others its full development is permitted, while in others, where it can run its full course, the diastole subsequently proceeds for a period silently. When I speak of early diastole, I should perhaps qualify this term. The murmur may be confined to early diastole, but more often it is in *delayed* early diastole, that is to say, there is a little gap between 2nd sound and murmur. Lastly, there may be no murmur although stenosis of slight or moderate grade is present; these cases are quite frequent.

I pass to a further discussion of the causation of the murmurs and especially to a working hypothesis which helps us to remember and to explain their variations under different conditions of heart action etcetera. First of all, I may sum up, making the chief statements in regard to the murmurs of mitral stenosis in tabular form. The table expresses the facts in broad outline.

Murmurs of Mitral Stenosis.

Heart	*Normal Rhythm*	*Auricular Fibrillation*
Action slow, stenosis slight.	Presystolic	No murmur.
Action slow, stenosis moderate.	Presystolic, perhaps also delayed early diastolic.	No murmur or delayed early diastolic.
Action slow, stenosis considerable.	Presystolic and delayed early diastolic, or full diastolic.	Constant delayed early diastolic with full diastolic for shorter diastoles.
Action rapid, stenosis slight.	Presystolic or more commonly full diastolic.	No murmur or more commonly a full diastolic.
Action rapid, stenosis greater.	Full diastolic.	Full diastolic; perhaps early diastolic only in longest diastoles.

It will be seen that a murmur may lie in presystole while the auricles fibrillate; so that it is not correct to say that a murmur is never found in this phase of the cardiac cycle under these conditions. It is correct to state that an *isolated* presystolic murmur is not found as an accompaniment of fibrillation. At all events this statement is true in the great majority of cases and at the most has exceptions in occasional single cycles in rare cases. If we scan the two columns of our table we remark that the murmurs accompanying the normal rhythm and those which accompany fibrillation differ only in one important respect; in fibrillation, as we might anticipate, such murmurs as may be attributed to auricular systole are not present. If this chief feature is remembered, and it is also remembered that the murmurs are less intense when the heart is failing and engorged, and that such engorgement is more apt to occur as an accompaniment of fibrillation than as an accompaniment of the normal rhythm, then the arrangement of the murmurs should be clear. How in a given case may the variations be explained? In the first two lines of Fig. 68 is a diagrammatic representation of simultaneous intra-auricular and intra-ventricular pressures. In the third line I have represented the differences in pressure between the two chambers. When the semilunar valves close (*S.C.* line) the pressure in the ventricles is still far above that in the auricles; the ventricular pressure is falling while the pressure in the auricle is rising for the blood is collecting in it. There comes a point when the auricular pressure exceeds the ventricular (*A-V-O* line) and at this point the *A-V* valves open, and the filling of the ventricle begins. The filling continues but gradually falls off in rate as it proceeds, for the pressure in the ventricle is rising, until at the end of diastole, and with the systole of the auricle, the auricular pressure rises suddenly and the filling is again hurried. In the normal heart cycle there are two periods of diastole during which filling is most rapid; these are the periods at which the differential pres-

sure is greatest on the auricular side; these are the periods at which the murmurs of stenosis are to be anticipated, for the murmurs are controlled by the rate at which the blood flows through the narrowed mitral orifice. I suggest that the pres-

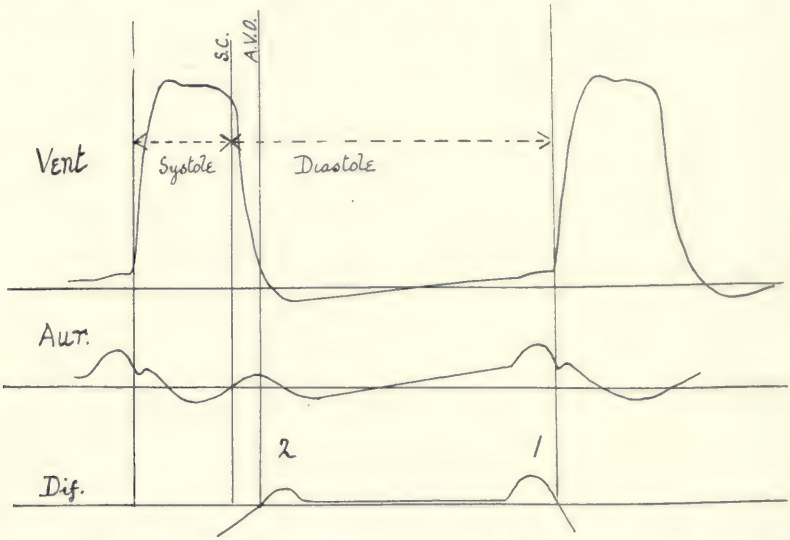


Fig. 68. A diagram of intracardiac pressures, to illustrate the influence of such pressures upon the murmurs of mitral stenosis.

ence or absence of a murmur is dependent upon the presence or absence of a critical rate of blood flow. In some cases the necessary rate is only reached in presystole. These are cases where filling is on the average slow, where the stenosis is slight and the auricles are active. If the stenosis is greater, the average rate of filling increases, so it does also if the heart rate increases, for this curtails diastole. As the average rate of filling increases, so the murmurs will become more manifest, and will appear not only in presystole, but at the period of next most rapid filling, namely, at the opening of the *A-V* valves. As the rate of filling becomes still faster the whole diastole will be noisy. In fibrillation cases the filling will occur

most rapidly at first; therefore the murmurs will be loudest in early diastole and, where diastole is long or stenosis moderate, may be confined to this period. This hypothesis sufficiently explains our observations; it also accounts for differences in the lengths and characters of the murmurs from one cycle to the next in a given case; the rate of filling varies with different phases of respiration, etc.; the hypothesis also accounts for variations in the murmurs in a given patient from day to day, for the blood flow varies in average rate, and the differential pressure curve varies in character from time to time and in different circumstances.

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Chapter IV

THIRD HERTER LECTURE

OBSERVATIONS UPON DYSPNŒA, WITH ESPECIAL REFERENCE TO ACIDOSIS

Gentlemen,

In my first two lectures I have considered two subjects, electrocardiography and phonography, using them to illustrate the value of precise laboratory methods in clinical observation. The third illustration, which forms our present topic, carries us farther afield. I propose to speak of certain recent observations upon dyspnœa, touching upon questions of chemical pathology.

The application of chemical pathology to clinical problems has been and still is sadly neglected. In the very near future this branch of medical science will be one of our greatest assets. I look forward to a time when no large institute for the treatment of patients will remain unprovided with a fully equipped chemical laboratory, controlled by skilled analysts; to a time when such a department will be deemed as indispensable as that of bacteriology. We can afford to neglect no channel of approach in studying the problems of disease. We must prepare for these innovations in method. If it is said that the simple bedside tests are of first importance to the practitioner, for these are alone available to him in his routine work, it may be replied that the laboratory and skilled assistance may be brought permanently within his reach. It is not and never can be wholly a question of facility; it must eventually be a question of the comparative merits of one or other method. Our conceptions of health and disease are the foundations upon which the happiness of the human race rests. Our present

expenditure in the advancement of medicine by research is as nothing to our outlay upon national and commercial enterprises.

Let me commence my present illustration by relating how my interest was first awakened in the chemistry of dyspnœa. It was by remarking upon the strange disproportion between cyanosis and breathlessness in given cases. Bring to mind those cases of congenital heart affection or of mitral stenosis in young people in which cyanosis is a most conspicuous feature; such patients may exhibit little breathlessness while they rest. Yet the oxygenation of the blood is evidently grossly deficient. Even deep cyanosis may be present while the respiratory rate is but little increased, the respiratory reserve but partially impaired. From this observation it may be argued that to produce urgent dyspnœa, the lack of oxygen, expressed clinically as cyanosis, must be extreme. Or, put from the other point of view, if dyspnœa be present and cyanosis absent, or if the cyanosis be not of equivalent grade, the dyspnœa is due wholly or partially to a cause other than deficient aeration of the blood.

Apply this argument clinically and I think you will be forced as I was forced to the view that a very large proportion of those patients who exhibit moderate or great distress of breathing, while they lie at rest in bed, are suffering from breathlessness which is due to causes other than lack of oxygen; the dyspnœa comes neither from an obstruction of the respiratory passages nor from defective circulation of the blood through the lungs. To what then is it due? In seeking an answer to this question, I requested, and was fortunate in securing the help of my friend, Mr. Barcroft, who has devoted many years of his life to laboratory researches upon gaseous exchange in the blood. Such results as I am able to relate are due to his collaboration, for the chief analytical work, the major task, has fallen to his share.

As the sequel will show, the dyspnœa described results from non-volatile acids in the blood. The method employed for the

detection of this increased acidity is a simple one and consists in estimating the degree of saturation of the blood with oxygen, when it is exposed to this gas at a known pressure and under given conditions. For, as Barcroft and his collaborators have shown, the combination of hæmoglobin with oxygen is materially influenced by the addition of minute quantities of acid or alkali. Acid diminishes, alkali increases the power of hæmoglobin to take up oxygen when it is exposed to this gas. Barcroft exposes to a definite pressure of oxygen a sample of whipped blood; the test is a delicate one; if the quantity of oxygen absorbed is known, the amount of acid which must be added to normal blood to produce a similar reaction may be calculated in percentage terms. If the same blood is exposed to oxygen in the presence of CO_2 at tensions equivalent to those found in the alveolar air of the patient from whom the blood is taken, the amount of oxygen absorbed gives a measure of the reaction of the blood as it circulates in the patient. The merits of this method are recognised by those who are in a position to judge of them. We may judge them ourselves by the results which are yielded. Mr. Barcroft working at Cambridge is able to calculate with remarkable accuracy, by examination of samples sent to him, the state of the respiration in patients whom he has never seen, patients bedded at our hospital in London.

It will be convenient to speak in the first instance of patients who have signs of cardiac disease. The observations have clearly shown that from such patients a distinct and large group may be separated at once, and that in this group the dyspnœa is associated with the presence of a non-volatile acid in the blood. The group consists of patients to whom I have already referred, where the degree of cyanosis is disproportioned to the respiratory distress. Before proceeding to a detailed statement of the symptom complex, we may briefly discuss the effects of blood reaction upon the respiratory centre. The blood

as you know is alkaline, it is always alkaline whether there is health or disease. When we speak of acidosis, we simply mean that the blood has a reduced alkalinity. Observation goes to show a remarkable sensitivity of the respiratory centre to variations in the blood reaction; so sensitive is it that it will respond to changes of reaction which are far beyond our most delicate titration tests. It has been shown that the introduction of very small quantities of acid or acid salt into the blood stream is followed by hyperpnœa (Leymann, etc.), and that the introduction of alkali produces apnœa. It is immaterial what the acid is; carbon dioxide acts in similar fashion to mineral or organic acid. Each produces its effect, according to the modern view, by increasing the number of free hydrogen ions in the blood. The response of the respiratory centre to blood reaction is the key to a clearer understanding of clinical dyspnœa. Dyspnœa resulting from increased hydrogen-ion concentration is of two kinds, it may come from volatile or non-volatile acids.

Simple mechanical dyspnœa.

If we examine relatively simple forms of cardiac disease, for example the mitral stenosis of young rheumatic girls, we find that such dyspnœa as is present may be accounted for by lack of oxygen and accumulation of CO_2; for the alveolar air, which samples the gases of the pulmonary capillaries, is deficient in oxygen and surcharged with CO_2 in these cases. Blood taken from these patients and freed from CO_2 has a normal alkalinity; there is no excess of non-volatile acid. The simplest form of cardiac dyspnœa is caused, therefore, by mechanical defect, an embarrassment of the circulation in the lungs. As a general rule such dyspnœa is not severe in patients who have been resting in bed; if cardiac patients continue to show great breathlessness another factor is generally discovered. Dyspnœa which comes from mechanical causes, be they primarily of circulatory, pulmonary or bronchial origin, proclaims itself clinically by its

attendant cyanosis. In cardiac patients who have this simple mechanical dyspnœa, venous and liver engorgement are the rule; such patients prefer to sit than to lie, for while lying the passage of venous blood from abdomen to heart is encouraged and the patients are, as a consequence, orthopnœic. If in these patients, you press upon the abdomen, the respiratory rate and volume at once become increased (Fig. 69). The same patients may com-

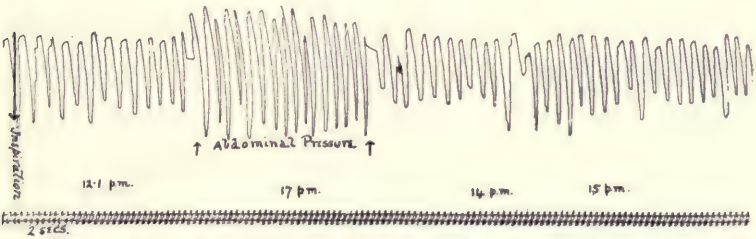

Fig. 69. A curve of respiration in a patient suffering from simple cardiac dyspnœa, showing the increase in the rate and depth of ventilation upon compressing the abdomen.

plain of aggravated breathlessness, which at night wakes them from sleep. This form of nocturnal breathlessness is to be clearly distinguished from a variety which I shall presently describe; it is due to the patients slipping down the bed from off their pillows.

The respiratory excursion is irregular in amplitude and in rhythm; reserve is reduced, so that the breath can be held but for a few seconds; forced breathing is followed not by apnœa as in the normal subject but by a resumption of the previous type of breathing or even by increased ventilation. Great distress is rarely witnessed in these relatively simple cases.

A special symptom complex.

The facts which I have just related will be familiar to you. This simple cardiac dyspnœa, in which the blood circulating through the brain is overladen with CO_2 is not difficult to recognise in frank cases. Neither is the second type, to which I

now pass, once you are acquainted with the clinical picture. I take first of all the most simple examples. There are patients, usually elderly, who are admitted to our wards and suffer from urgent dyspnœa. The breathing is laboured; it is periodic and of the Cheyne-Stokes type (Fig. 70). The patients are not orthopnœic, they exhibit few signs of venous or liver engorgement, pressure upon the abdomen does not materially increase the depth or rate of respiration (Fig. 71). *The uncomplicated cases are not cyanosed.* The blood is fully aerated and has a low tension of CO_2. There is little or no reserve. The administration of oxygen affords practically no relief. A conspicuous feature is the presence of nocturnal attacks of breathlessness, and these wake the patients repeatedly from slumber, are often suffocative and last from a few minutes to half an hour or more. The heart is a little dilated; the pulse rate is almost always increased (80-100) and especially towards

Fig. 70. Two examples of Cheyne-Stokes breathing from cases exhibiting nonvolatile acidosis.

evening. The temperature is generally subnormal. The blood after removal of its CO_2 shows a considerable decrease of alkalinity, which is due to the excessive presence of non-volatile acids or acid salts.

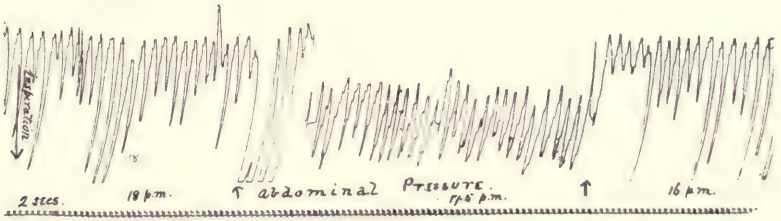

Fig. 71. A curve of respiration in a patient suffering from slight non-volatile acidosis. Pressure upon the abdomen does not increase the respirations in rate or depth.

These are the almost constant clinical manifestations, but the picture is varied in a hundred ways. Add to it the symptoms and signs of heart disease in its various forms; add to it the symptoms and signs of renal disease and its complications, add emphysema, or cerebral arterial disease, and you are able to reconstruct the protean types in which this curious acidosis is displayed. It may be that you will declare the special symptom complex which I describe to you as uræmic, that may or may not be justified; I have deliberately avoided this term on account of its laxity. There is of course no question but that many of the cases which I have in mind are commonly termed uræmic; for the urine is of low specific gravity and contains albumen and granular casts; the blood pressure is often high; and other so-called "uræmic manifestations" frequently appear. Severe headache, twitching of the limbs, vomiting, temporary hemiplegia, convulsive seizures or aphasia may appear. Thirst and anorexia are common; wasting and a little anæmia are frequent; inflammatory affections of lung and pleura are frequent terminal complications. But what I wish to impress is that none of these last named symptoms is essential to the complex, any more than are those cardiac symptoms which I shall pres-

ently describe essential. Uræmic dyspnœa is a term which we should carefully avoid, for it presupposes that the breathlessness is primarily of renal origin; of this we are not certain at the present time. The malady and its varieties can only be appreciated fully if the essential features are isolated or constantly maintained in relief. They are those I have already enumerated, and which I now repeat, namely, dyspnœa in the absence of cyanosis or an equivalent cyanosis, accompanied by periodicity of respiration and by nocturnal seizures; some dilatation of the heart, rapid pulse action and a subnormal temperature. Lastly, there are the characters of the alveolar air, the high oxygen and low CO_2 content, and the signs of a non-volatile acid in the blood.

The remaining signs and symptoms are not essential features, but one or other, or several, are almost always present. The uncomplicated case is rare. It is to this fact that the protean character of the malady is due; it is to this fact that the symptom complex has remained hidden in the past, for it is usually obscured in greater or lesser degree. Nothing tends to hide it more than the presence of cardiac failure, and this is an extremely frequent complication. The heart may be affected in a variety of ways. Any valve lesion may be present, aortic dilatation or actual aneurysm are not uncommon. You may find all varieties of altered heart mechanism; fibrillation of the auricles and pulsus alternans are especially frequent. Anginal pains may be present. Engorgement of the veins and liver, with or without ascites and dropsy, are the rule rather than the exception in advanced cases.

These superadded phenomena mask an otherwise obvious condition; engorgement of the venous system especially embarrasses the diagnosis, for it veils or hides the all important discrepancy between the breathlessness and the oxygenation of the blood. Many of these unfortunate people suffer not only from a fixed acidosis but in addition from the simple form of cardiac dyspnœa, due to lack of blood aeration. Generally speak-

ing, the whole trouble of breathing is referred to the last named cause; for where the pulmonary circulation is evidently defective, where in the presence of slight or moderate cyanosis, signs of aneurysm, of emphysema, or of venous engorgement, are found, the temptation to ascribe the whole breathlessness to a purely mechanical cause is too often irresistible. That the mechanical cause is not the sole cause, that often it is not even the chief cause, has been clearly shown by the blood tests. We become more and more convinced as these tests increase in number that there are very few inmates of our hospitals who suffer from really urgent and constant breathlessness, in whom a mechanical hypothesis is sufficient to explain the symptoms. You are familiar with those distressing cases, patients of middle or advanced years, who in a semi-conscious state, sit in chairs in our wards, and while cyanosed and dropsical, struggle for breath during the rest of their existences. It may be that mitral stenosis, it may be that aortic disease or aneurysm are present. It may be that bronchitis and emphysema are diagnosed. In each and all in our experience a non-volatile acidosis is a chief trouble. The more we see of the blood reactions, the more mechanical dyspnœa recedes to the background. The secret of the clinical diagnosis lies in a nice discrimination between the degree of breathlessness and the degree of cyanosis, in a mental comparison between these patients and those cases of mitral stenosis or congenital heart disease in which there is an obvious lack of blood aeration.

Our tests show quite clearly that if a very breathless patient has but slight or moderate cyanosis, whether or no such patient is afflicted with emphysema, myocardial or valvular heart disease, aneurysm of the aortic arch or what not, the breathlessness cannot be ascribed wholly to a mechanical cause. In the light of laboratory observation the old faiths fall away fast. Stronger and stronger becomes the conviction that death from actual but gradual asphyxia in an uncomplicated form is a rare event in

our patients, and that by far the commonest form of urgent breathlessness is the acidosis which I am describing to you. Go into the wards of a general hospital; you will rarely fail to see a number of sufferers sitting in bed and in urgent need of breath; three-fourths at least of such cases are examples of the condition now considered.

Their diseases are partially described by a variety of diagnosis; angina pectoris, aortic disease, aneurysm, mitral regurgitation, mitral stenosis, arterial disease, chronic bronchitis, uræmia, cardiac asthma, coronary arterial disease, hydrothorax or pleurisy. In each and all of these conditions, acidosis may be found as an association, when the laboratory tests are undertaken.

Where the breathlessness is due to non-volatile acids only, then the respiratory embarrassment is proportioned to the degree of acidity. When such patients improve the acidity is found to decline; as they lose their breathlessness, the blood reaction becomes normal. The chemical test is a sensitive laboratory indication of the patients' respiratory exchange.

Where heart failure is added, then the breathlessness is governed by two factors, first by the quantity of non-volatile acid present, and secondly by the degree of deficiency in aeration. The two combine to a common end, the creation of hyperpnœa. The most urgent dyspnœas belong to this group.

It is also to be noticed that the presence of a slight grade of relative acidity, although it may not in itself give rise to prominent dyspnœa, limits the reserve, so that any influence, such as exercise, holding the breath, etc., which is followed by increased ventilation in normal subjects, acts in these subjects with exaggerated effect. The field of respiratory response is strictly limited and its bounds are easily crossed by these people.

Other conditions in which non-volatile acidosis has been found.

I have sketched for you the type of case where you may most

readily and surely find the acidosis in question. There are other conditions in which it is known to exist. The simplest example is physiological, the dyspnœa of violent and prolonged exercise is due to such a cause; here too there is no cyanosis and the acid responsible has proved to be lactic acid, formed in the contracting muscles. In the increased ventilation of the lungs of diabetes, the alveolar air contains more oxygen and less CO_2 than normal. The hyperpnœa is not due to lack of oxygenation but to decreased blood alkalinity, owing to the presence of oxybutyric and diacetic acids. On account of this relative acidity the respiratory centre is stimulated, ventilation is increased, the CO_2 in the blood is decreased, oxygen is increased. In this manner, a partial compensation is established. But reserve is diminished. A similar condition is discovered in normal subjects at high altitudes, though the nature of the acid has not been identified as yet. In two of the patients in our own series, lactic acid was found in excess in the blood by Dr. Ryffel, but both these patients were at the time moribund and we cannot regard it as the invariable or even the common malefactor; the usual acid is again unknown.

Recently we have extended our search amongst clinical cases and have found a similar acidosis in a number of conditions in which it was formerly unsuspected. These observations have not been published, but I have Mr. Barcroft's permission to speak of them. It is present in acute lobar pneumonia and is largely responsible for the dyspnœa which accompanies this consolidation of the lung tissue. The acidosis may be of high grade, in which case the patients in our experience do not recover. Where it is originally of slighter grade, it persists over the crisis to vanish hand in hand with the breathlessness as the patient becomes convalescent. In view of these facts, we are no longer justified in attributing the whole breathlessness of pneumonia to the lung damage; a statement which is supported by the fact that pneumococcal lesions in other parts of the body may also

be associated with breathlessness. We have recently found a similar acidosis in a case of exophthalmic goitre, where with other toxic symptoms, such as vomiting and mania, breathlessness was distressing. Not so long ago a patient was admitted to hospital having developed an acute pneumothorax, a secondary result of chronic but almost quiescent tuberculosis. He showed dyspnœa which varied in its intensity; the blood reaction presented similar variations, being more on the acid side while the dyspnœa was great, and more on the alkaline side while the dyspnœa was slight or absent. This instance is of special interest, for with unquestionable signs of collapse in one lung, and in the absence of chemical tests, we should have had no hesitation in ascribing the respiratory disturbance to a mechanical cause. Yet the chief cause was not mechanical but toxic. Of cases of mitral stenosis in early years, we have examined a number; in all but one of these patients acidosis was absent. The solitary exception was a young woman, a primi-gravida at full term. Here acidosis was present in considerable degree and granular casts were discovered in the urine.

Gentlemen, the observations are still at an early stage, but they are full of promise. There is in fact no branch of clinical pathology of which I know which offers greater opportunities for earnest workers at the present time. There is a wide field for research. The requisite laboratory methods are at our disposal; we have but to apply them to our clinical material to reap a rich harvest of new facts. One conclusion should be emphasised. We are not justified at the present time in ascribing dyspnœa to a mechanical cause, to deficient aeration of the blood, except in the most simple forms of cardiac breathlessness, or where an evident obstruction to the respiratory passages is the only lesion in the patient. Non-volatile acids, as opposed to CO_2, appear to be an almost universal cause. There seems to me to be little doubt that all forms of so called renal dyspnœa, many forms of cardiac dyspnœa, and many of the dyspnœas which have in the

past been ascribed to pressure by tumours, such as an aneurysm, or to consolidation of the lung, collapse or emphysema of the same organ, are produced in reality mainly through the products of altered metabolism.

Renal dyspnœa.

At an earlier stage I described in some detail a symptom complex in elderly subjects, where Cheyne-Stokes breathing and nocturnal breathlessness are prominent symptoms. The question as to whether we must regard such breathlessness as of renal origin in these patients is still an open one. All present signs of renal involvement, those who have come to autopsy have demonstrated renal lesions; all also present symptoms of cardiac affection. Most of those examined after death disclose coronary arterial disease and a degenerate myocardium. We require analyses in cases of a purer kind; especially we require investigation of those comparatively rare cases of dyspnœa in young subjects where the kidneys are shrunken and pale. A single case of parenchymatous nephritis is included in our series; it was a man who died with universal dropsy of frank renal type. The acidosis was in his case extreme and the breathlessness very urgent. A most suggestive observation, but unhappily not uncomplicated, for at autopsy a certain grade of aortic and mitral mischief was also discovered. We require observations upon pure eclampsia too before a full answer can be returned. Instances of breathlessness resulting from acidosis in patients described as uræmic have been separately and recently reported by Ryffel and Poulton, but their description and the consequent suggestion that the dyspnœa was of renal origin should not be accepted before we have full clinical details of their cases; the cases which they describe were in all probability of the same type as those included in the series upon which my present observations are based. The same statement applies to Straub and Schleyer's patients in whom a decreased CO_2 content was

discovered in the alveolar air. This change in constitution of the alveolar air was rightly regarded by them as evidence of decreased alkalinity of the blood.

Our first task is the isolation of all the clinical types in which dyspnœa has its origin in acidosis. It were wiser in investigations of this kind that the actual facts in regard to the patients observed should be given in full detail. To tabulate the cases under such broad and ill-defined headings as uræmia and to leave them at that is in the long run a waste of valuable material. That uræmia was present is a matter of opinion, as the meaning of a term which still lacks definition is also a matter of opinion.

The second task, which must fall purely to the lot of the chemist, is the identification of the substance or substances responsible. When we have this information, we shall be in a position to investigate and discuss the seat of the disorder, and to approach its treatment with greater prospect of success. At present the renal origin of dyspnœa is chiefly a matter of speculation; therefore I do not propose to enter further upon its discussion.

Periodic breathlessness.

In conclusion, may I refer to certain forms of periodic breathlessness. Quite recently a patient came to my out-patient department for an examination of the heart. A man of 50 years, of florid appearance, who presented signs of a little cardiac enlargement, and exhibited upon examination some very slight breathlessness. Other physical signs were few. During the course of his examination, he became abruptly dyspnœic and within a few moments had passed into a condition of the utmost gravity. Breathlessness was the primary symptom, the respiratory rate rose to 44 per minute; later he became cyanosed, eventually deeply cyanosed, the temperature fell below 96°, the pulse increased to 140, the expanded chest was filled with

rhonchi. There was no expectoration, but large quantities of urine were voided, the face and limbs were pale and cold, the brow clammy. The whole attack, lasting but a few hours, gave rise to grave anxiety for his life. A sample of blood taken during the attack showed a profound acidosis. The recovery was almost as speedy as the onset; and samples of blood examined within the next few days told us that its reaction had returned almost to normality. The attack was one of two which the patient had experienced. Apparently the blood had of a sudden suffered invasion by acid products in sufficient quantity to bring life into immediate jeopardy. What was the cause of this flooding of the system? We do not know. Some would call it an attack of cardiac or renal asthma; preferably we confine ourselves to the known fact that the crisis was produced by the invasion of the system by acid products. We require many more observations of a similar kind, we require them not only in cases suspected of renal or cardiac disability, but in every type of case in which such paroxysmal seizures are to be found. It may or may not be that there is a condition in which the bronchioles become suddenly constricted, the old bronchial asthma; we have no direct proof, though we have strong presumptive evidence of such a pathology. If you are prepared to accept the observations which I have put before you, you will agree that the whole question of asthma has to be revised. There are too the special nocturnal attacks of breathlessness to which elderly patients are subject; we require special observations upon these cases at the times of such attacks.

My plea is not that you will accept the views which I have put forward in their entirety, but that you should recognise how much there is still to learn on the question of dyspnœa; the time has come when, with precise methods at our disposal, we must pause until such knowledge as these methods may produce is acquired, suspending judgment meanwhile, but frankly ac-

knowledging that the whole pathology of constant and of periodic dyspnœa enters upon a new phase, and that the faiths to which we have adhered in the past, may not command our support in the future.

At our feet lie pick and spade; this plot of land cries out to us to take them up and bury them in its virgin soil.

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AN ADDRESS

ENTITLED

"OBSERVATIONS UPON CARDIAC SYNCOPE"

Delivered at the Opening of the Faculty of Medicine, McGill University, Montreal, October 5th, 1914.

Chapter V

OBSERVATIONS UPON CARDIAC SYNCOPE

Gentlemen,

In responding to the invitation which you have done me the honour of sending me, I have chosen " Cardiac Syncope " as the subject of my remarks to-day.

There is a common misconception at the present day that the study of the heart's action by modern means finishes and ends with disorder of the heart beat; that indications of systole of the auricles and ventricles, obtained directly or indirectly by mechanical or electrical means, are simply of value in interpreting and classifying irregularities of the pulse or heart.

The electrocardiograph and the polygraph, recent devices for graphic registration, should be regarded rather as individual means to a specific end, research upon human pathology in all its phases and by the most accurate methods which may be employed. While the nature of disordered heart action is a study rapidly reaching its termination, the problems which such study has opened up are manifold and far reaching. Our general conceptions of heart disease are rapidly and surely altering, and this change in our processes of thought has been governed largely, if not entirely, by the widespread adoption of the graphic method. The method, by its precision, has sharpened our critical faculties; it has insistently emphasised the value of close observation upon the actual events of disease; in short, it has created in this field of work an atmosphere of refinement and exactitude, the influence of which at present dominates, and will in the future dominate the world of cardiac pathology. It has carried this branch of clinical science in one step to the level

of its companion sciences of the laboratory; it has awakened a great and growing dissatisfaction with traditional cardiac philosophy. Our new philosophy is deeply rooted, it is to be trained to cover a hard and imperishable wall of fact; the old philosophy entwines a neighbouring trellis whose frailty assumes increasing prominence. Graphic experience has clearly displayed the insufficiency and the weaknesses of the older methods; has stressed the need of searching revision; has more narrowly defined the bounds of legitimate argument; has condemned those flights of imagination which have been responsible in the past for precarious conceptions, for loose reasoning; has reminded us in unmistakable language that facts are our only sure foothold, the only real estate which we bequeath to our successors; has warned us once again to realise that hypothesis is but a guide to observation, and that dogma has no place in the pursuit of knowledge.

My purpose in the present address is to take one of many possible illustrations and to attempt to show you where our true knowledge and our legitimate conceptions of the pathology of cardiac syncope begin and end.

It is advisable that I define for you at the outset what I intend to convey in the present address by the term "cardiac syncope"; I wish to convey a sudden loss of consciousness which is due to a derangement of the heart's function. We may pause for a few moments to consider the limits of this definition. On the one hand, and considered strictly, it excludes such symptoms as are described by our patients as "faintness" or "giddiness." These symptoms, as you are aware, are common manifestations of heart disease; not infrequently they are produced in a manner similar to real cardiac syncope as I have defined it. That is to say a momentary faintness or giddiness may result from a cause of identical nature with that which induces loss of consciousness, though in the last case the disturbance is of longer duration. To some extent, therefore, we cannot refrain from alluding to these symptoms; we may refrain just

in so far as may be necessary to maintain the discussion within convenient limits; thus I do not propose to consider the attacks of faintness or giddiness which are specially associated with aortic disease. On the other hand, our definition will include many forms of unexpected death in cardiac patients, for such death as we shall see may come as a natural sequence of events which first induce simple loss of consciousness.

Again, our definition will exclude all possible causes of syncope in which the arterial system is the prime malefactor. Cerebral arterial disease is a subject which I shall not consider. Neither will it be possible more than to refer in passing to one of the commonest forms of syncope, namely, fainting attacks in young people; I mean those attacks which are universally and probably rightly attributed to vasomotor disturbances in the splanchnic area. Briefly, we shall concentrate our attention upon the heart itself, enquiring especially into the nature of attacks of unconsciousness which are unquestionably associated with disordered rhythm or into the nature of unexpected death supposedly of similar origin.

Causes of cardiac syncope and unexpected deaths of cardiac origin.

Amongst the causes of sudden and unexpected death of cardiac origin there are several which have been completely understood for a long while. Embolic plugging of the pulmonary artery and impaction of a ball thrombus in a narrowed mitral orifice are recognised causes of such death; in each instance the chief channel is abruptly and completely obstructed and the circulation is brought to an immediate standstill. In hospital patients, in whom there has been a sudden catastrophe, a third cause is always sought at autopsy, namely, plugging of a main coronary artery or a chief branch. Upon this accident I shall have more to say presently. Another terminal event is rupture of the heart wall, or rupture of an aortic aneurism into the pericardium

or pulmonary artery. These causes of unexpected death are, for the most part mechanical, and on that account have appealed forcibly to pathologists in the past; for they are capable of demonstration in the post-mortem room. But how often does the examination proceed to its termination upon the bodies of patients who have collapsed unexpectedly, without the discovery of the cause of death? In the majority of patients who have died of cardiac syncope in the past, no lesion has been found which could be said to be directly responsible. It is precisely this type of syncope to which I propose to devote chief attention; and for several reasons. In the first place, because it begins to be more fully understood; in the second place, because by its study we may be forewarned of its approach in given cases and may adopt suitable measures for its prevention. You will find a good deal has been said, but that little or nothing has been known concerning sudden *diastolic arrest* of the heart, or, as the French physicians term it, *asystole*. These terms mean no more than that the heart ceases to beat.

You will read of spasm or cramp of the muscle, conditions unknown to physiology; equally unknown to pathology. You will all have heard accounts of patients who succumb to a mysterious malady, *angina sine dolore*. Such terms bring us no nearer the truth; give us no clearer conception of the cause of death.

The causes of unexpected death are to be discovered by laboratory experiment, and especially by observations upon recurrent cardiac syncope in the human being. It is to the last source that we owe most of our knowledge to-day. What then do we know positively of cardiac syncope? We know that it may be produced in a variety of ways, which may be classed under two broad headlines, (1) retardation or cessation of the ventricular action; (2) acceleration of the ventricular beating. Under the first heading we may consider (*a*) slowing or standstill of the whole heart (*b*) slowing or standstill of the ventricle.

Under the same heading we may discuss (*c*) ventricular fibrillation.

Slowing or standstill of the whole heart.

There are now a number of cases upon record in which attacks of cardiac syncope may be definitely ascribed to standstill of the whole heart. The most perfect example of its kind was described by Laslett a few years ago. The syncopal attacks were associated with intermissions of the heart action of 4-8 seconds duration. An example of the curves, which demonstrate cessation of both auricular and ventricular action, is seen in Fig. 72, which is from this case. The attacks were fre-

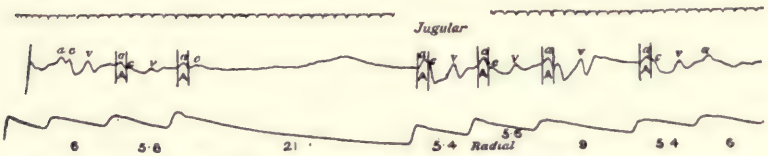

Fig. 72. Venous and radial curves during a syncopal attack, due to vagal standstill of the whole heart. (After Laslett.)

quently repeated, sometimes at intervals of a few moments; almost certainly they were produced through the medium of the vagus, for atropine abolished them.

A case which probably belongs to the same category has been recorded by Neubürger and Edinger. Frequent syncopal attacks, in which the pulse failed, were observed in a man who, at autopsy, exhibited a small aneurism upon the basilar artery; the attacks came with effort, or at such times as a rise of blood pressure might be held to account for enlargement of the tumour with pressure on the vagal centre in the medulla. This patient succumbed to a seizure of the kind. Their report is most suggestive and striking, and it is only to be regretted that at the time graphic methods had not sufficiently developed.

Syncope which is the result of standstill of the whole heart is a rare phenomenon.

Standstill of the ventricle.

A more frequent cause of cardiac syncope is standstill of the ventricle, the auricle continuing to beat at about its former rate; this event is associated with heart-block. It is convenient in dealing with this subject to sub-group the clinical cases.

Sudden development of heart-block. Syncope may come without warning in patients who present a perfectly normal heart mechanism up to the time of the attack. For illustration of this form of seizure I may cite a case which recently came under my care. A man of 48 years, suffering from chronic aortic stenosis, had for some years experienced attacks of giddiness followed often by a temporary lapse of consciousness; they came without warning, and sometimes he fell heavily. When seen, the attacks were of irregular frequence, but numerous, ranging in number from one or two to several hundred in the day. On several occasions I talked to him while he sat in a chair, and from time to time, as he replied to my questions, a sudden and intense pallor overspread his features; he became abruptly silent, the pupils dilated, respiration deepened and a little squint and general rigidity developed; consciousness might or might not be lost momentarily. In a little, the face became intensely flushed, he moved and gradually regained complete mental control. An example of the curves, showing the events accompanying two attacks, is given in Fig. 73.

The mechanism of the heart, before and after the attack was perfectly natural; during the attack the pulse failed for a period of 3 to 8 seconds; a lapse of 5 seconds was sufficient to abolish consciousness. During the period of standstill, the heart sounds were in abeyance, but the auricles continued to beat at their former rate. The offset was accompanied by accelerated heart action and a rapid rise of blood pressure. In this patient atropine failed to give relief. In the absence of a cellular examination of the heart, the cause of the heart-

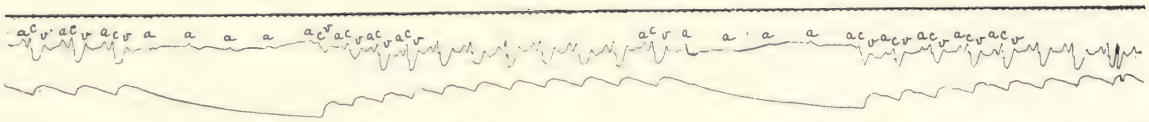

Fig. 73. Venous and radial curves showing the nature of two brief syncopal attacks. They were due to the sudden onset of heart-block, and standstill of the ventricle.

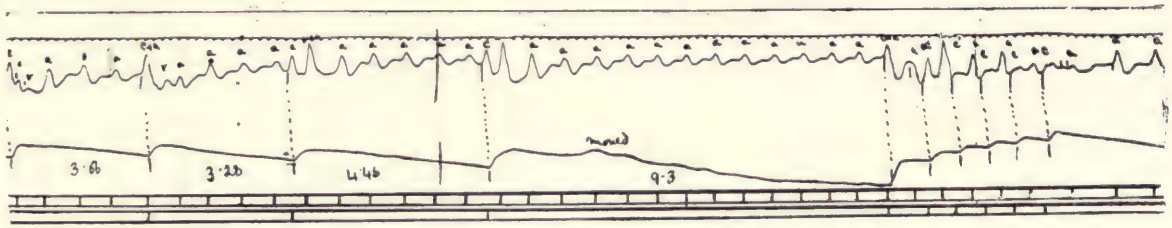

Fig. 74. Venous and radial curves from a case of complete heart-block showing standstill of the ventricle while the auricle continues to beat. (After K. D. Wilkinson, "On the Value in Clinical Medicine of Graphic Methods," etc., Birmingham, 1912.)

block cannot be defined accurately, but as the patient has more recently developed complete dissociation of the auricles and ventricles, it seems probable that a lesion of the *A-V* bundle was responsible for them. Some years ago I saw a somewhat similar case; in this instance fits came in groups between intervals of freedom which lasted several months; on the days when they were experienced, partial heart-block of low grade was found. This patient died as a result of a fall during an attack and Dr. Cohn examined the heart for me. He found large blood sinuses in the *A-V* bundle, the tissue having almost the appearance of a nævus; it is easy to comprehend how in this instance an added strain with engorgement of those vessels would bring about cessation of the ventricular beating.

Increase of pre-existing block. Syncope is a very frequent accident in patients who are the subjects of chronic partial heart-block, where for example the auricles beat at exactly twice the rate of the ventricles; in all such cases it is due to a sudden increase in the degree of block, the ventricle, which originally responded to alternate auricular impulses, remaining inert for a variable period.

Two explanations of the sudden exaggeration of the conduction defect in these patients have been put forward. In some instances, for example in the case reported by Erlanger, the ventricular silence was preceded by a period of auricular quickening. Now when partial heart-block is present, its degree is enhanced by acceleration of the auricles, and the net result is a fall of ventricular rate which may amount to a standstill. It may be, therefore, that the fits of partial heart-block are produced in this manner in some patients. It has also been supposed that the exaggerated block is produced by vagal influences; undoubtedly the vagus is capable of producing this increase of block, as has been shown by Rihl and others who have occasioned fits in these patients by pressing upon the vagus in the neck; but the effects of atropine are uncertain and too

often negative. The actual provocative cause in most cases is still unknown.

Ventricular standstill in complete heart-block. The highest grade of heart-block is that in which auricle and ventricle are dissociated, each beating regularly and at its own inherent rate. In such patients, the auricular rate is 70 per minute or a little higher; the ventricular rhythm has a usual rate of 30 to 40 per minute; this rhythm is developed in the ventricle itself, and in all probability in the auriculo-ventricular bundle. These patients are by no means exempt from syncopal attacks; the majority suffer from them. Here too, the fits are the result of ventricular stoppage (Fig 74). Erlanger and Blackman have succeeded in reviving dogs after crushing the *A-V* bundle, and in several of these animals characteristic syncopal attacks developed. Now although the vagus has an undoubted influence upon the mammalian ventricle, it is improbable that this nerve can be held responsible for the additional ventricular slowing; for fits could not be produced by stimulation of the vagus in Erlanger's experiments; and there is a growing consensus of opinion that the influence of the vagus upon the ventricle, *dissociated from the auricles by lesion,* is slight; it seems probable that most of the vagal fibres run to the ventricle along the same tract as the auriculo-ventricular muscle fibres. Attention directs itself therefore to the centre which forms the independent ventricular rhythm, and especially to its nutrition. The centre is localised in the main stem of the bundle immediately below the lesion which produces the original heart-block. This tissue is often diseased in the patients whom we are considering; that is to say the tissue upon which the ventricle depends for its rhythm is presumed to be in an abnormal state; little wonder, in such circumstances, if rhythm production in this region is from time to time impaired. A single case has been recorded in which the fits of complete heart-block received complete explanation. The independent ventricular rhythm is influenced in a notable

fashion by stimulation of the ventricle. Originally slow, its rate may be artificially enhanced by interrupted stimulation, and a higher rate of beating may be maintained in this fashion over indefinite periods; but if at any time stimulation ceases, the independent rhythm shows unwillingness to return: it takes time to develop and prolonged standstill results. In a patient who was the subject of complete heart block, the ventricular rate was constantly 30 per minute, but from time to time a new rhythm of extra-systolic nature developed, driving the ventricle at 70 or more per minute. At the cessation of this rhythm, standstill of the ventricle, associated with syncope (and in the last attacks with syncope terminating in death) was the rule.

A chart of the ventricular beats in this patient, constructed from curves taken over a long period, is shown in Fig. 75.

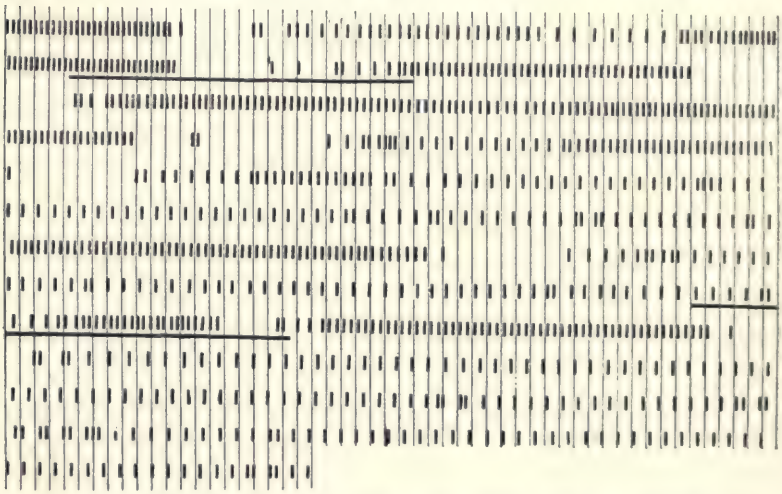

Fig. 75. A diagram compiled from a continuous curve of the apex beat, the duration of which was 21 minutes. The diagram reads from left to right, following consecutive lines. Each beat of the original curve has been charted on a large scale and the chart has been reduced subsequently photographically. The vertical lines are placed at two-second intervals. The relation of the (relative) tachycardial periods to the long asystolic intervals is very clearly shown.

The relation of standstill to the preceding acceleration of ventricular rate is clearly shown in this diagram.

Cerebral anæmia and its effects. In the forms of cardiac syncope which we have considered the output from the left ventricle is diminished and arterial blood pressure falls almost to zero; the subjective manifestations are the result of cerebral anæmia. The events which follow defective blood supply to the brain, are well known; severe hæmorrhage is quickly followed by loss of consciousness; in the slaughtering of sheep the carotids are severed, the animals fall unconscious almost immediately and after a little while convulsive movements are exhibited. Kussmaul and Tenner compressed the carotid arteries in a number of male adults; pallor of the face followed and the pupils dilated; "as soon as the dilatation of the pupils began to take place, the respirations became slow, deep, and as it were sighing. Afterwards dizziness, staggering and unconsciousness ensued." In two instances vomiting and convulsions were noted as compression was continued. Schiff and Hill have produced unilateral convulsions by the compression of one carotid.

You are aware that consciousness is often lost in hutch rabbits if they are held a short while by the ears and that this is due to an effect of gravity, namely to accumulation of blood in the abdomen. In a number of patients, when the abdominal walls are lax, momentary giddiness may be caused by sudden assumption of the erect posture; in those who complain of this symptom, rising to the erect posture is associated with a demonstrable and considerable fall of blood pressure.

It was Webster who first showed that in Adams-Stokes syndrome the fit is preceded by pulse slowing; and since his time the events of the fit have been carefully studied, especially in cases of heart-block. Cessation of the ventricular contraction comes first, and is speedily succeeded by general pallor of the skin; dilatation of the pupils, giddiness and dimness of vision quickly follow; if the ventricular silence is continued, conscious-

ness is lost and epileptic phenomena consisting chiefly of twitchings of the facial muscles, movements of the eye-balls and jerking of the upper limbs are added. In a few cases the convulsion becomes general, but the movements are rarely violent. The objective signs of venous stains complicate the picture when the fit lasts. Termination in death is not infrequent. The character of the attack is controlled in the main by its duration, recovery may come at any stage, and is preceded by a return of the pulse beats. The nervous phenomena witnessed in these syncopal attacks are entirely accounted for by cerebral anæmia resulting from cessation of the circulation. If we study the accounts which have been published, we shall find that although there are notable individual idiosyncrasies, standstill of the ventricle for a period of 3-5 seconds usually produces unconsciousness; at the end of 15-20 seconds epilepsy commences; an absence of ventricular contraction for 90-120 seconds is rarely followed by recovery.

Although abrupt cessation of the ventricular beating is the rule in these forms of syncope, simple slowing may be responsible for it. A fall of heart rate to a range of from 8-15 beats per minute is rarely tolerated without the patient passing into a condition of coma.

Fibrillation of the ventricles.

It is a remarkable fact that practically every form of irregularity, which has been produced experimentally in the mammalian heart, has now been recorded frequently in clinical cases. But there is one notable exception. We know that the rhythmic contraction of the human auricle is often disturbed by extrasystoles, paroxysms of rapid action and fibrillation; we know that the experimental ventricle is subject to parallel disorders, and that extrasystoles and rapid action may originate in the human ventricle; but with one or two rare instances, fibrillation of this chamber has not been witnessed clinically. Fibrillation

of the human auricles has been proved beyond doubt to be the most frequent cause of disordered heart action; why is fibrillation of the ventricle so uncommon an experience? For a good reason: Fibrillation of the ventricles is incompatible with existence. When the ventricles fibrillate, the co-ordinate beat of these chambers is lost; the muscle is divided up into small areas, which show independent activities; as a result the output of the heart ceases abruptly, the blood pressure falls to zero, the circulation is at a standstill. In other words, fibrillation of the ventricle, if it occurs in man, is responsible for unexpected and sudden death.*

We have the strongest *a priori* grounds for the belief that sudden death comes in this way in many patients.†

Unexpected death in cases of fibrillation of the auricle.

Sudden and unexpected death, attributable to this cause, is most common amongst heart patients who present fibrillation of the auricles. It is a not infrequent termination in these patients; the conditions necessary to persistent fibrillation of the auricles are present and it is largely for this reason that the form of death which I shall describe to you is attributed to fibrillation of the ventricles. These patients are often admitted to hospital suffering from all the classical signs of cardiac failure; they are treated with digitalis, often in considerable doses, and react admirably to this drug, for the ventricular rate slows, while breathlessness, cyanosis, venous and liver engorgement and dropsy subside or vanish. From time to time a sudden and unexpected catastrophe happens; regarded as con-

* In some animals, fibrillation may be a temporary event; but this is rare and is seen chiefly in the rat, rabbit and cat. In the dog, fibrillation is nearly always terminal.

† The suggestion that fibrillation of the ventricles may be responsible for sudden death was first made by MacWilliam; I made the same suggestion five years ago in writing on auricular fibrillation. Hering and others have since adopted the same view.

Fig. 76. Venous and radial curves showing digitalis coupling. The coupled beats in the arterial curves are separated by uneven pauses.

valescent the patient is sitting in bed, chatting or feeding may be. A nurse in charge or perhaps a neighbouring patient hears a cry or choking sound; the patient falls back on the pillows intensely pale, there are a few gasping respirations, a little convulsive movement, and the pulseless patient, rapidly becoming livid, is still. These are the symptoms which follow when fibrillation develops in an experimental animal; it is hardly to be doubted, considering the circumstances, that the same event terminates the life of the patient.

The fatal accident may happen in the untreated disease, or it may happen when any drug of the digitalis group (strophanthine, etc.) is given in excess; the same drugs given in poisonous doses to animals will induce ventricular fibrillation. In the administration of digitalis in cases of auricular fibrillation the period of danger is marked by the appearance of a bigeminal pulse (Fig. 76); upon analysis this bigeminy is found to result from extrasystoles of ventricular origin, beats which are frequent precursors of fibrillation in experiment.

A few isolated instances of curves purporting to show fibrillation of the ventricles in the human subject have been published. In one of several curves recorded by Robinson and

Draper from moribund or dead patients, fibrillation is depicted. Hoffman has recorded an instance of syncope in which the electrocardiograms are interpreted in the same fashion, but the analyses of these curves are open to question. The actual events in unexpected death are still in a measure uncertain; nevertheless the assumption of ventricular fibrillation is strongly supported.*

Death from chloroform. Recently some remarkable observa-

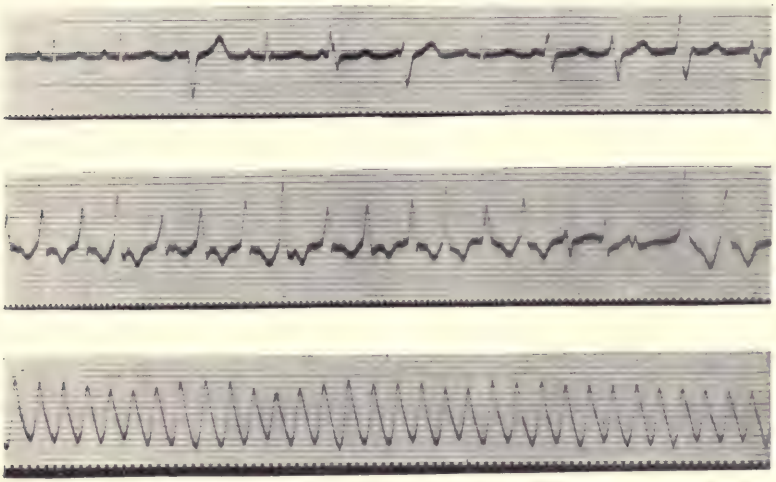

Fig. 77. Three electrocardiograms from a cat anæsthetised with a weak chloroform vapour. After a minute dose of adrenalin extrasystoles of ventricular origin appeared (*a*). These became more frequent until the heart responded entirely to new impulses of ventricular origin (*b*). In a short while fibrillation commenced (*c*).

tions have been made by Levy. He has shown in a very conclusive manner that death during the administration of chloroform to cats is almost always due to the onset of this curious derangement of the heart beat and that it comes when the heart is rendered suspectible by *small* percentages of the vapour (Fig. 77). Levy goes further and makes out an extremely strong case for his view that the majority of chloroform fatalities in the

* Dr. Halsey of New York has recently shown me a convincing example of death from fibrillation.

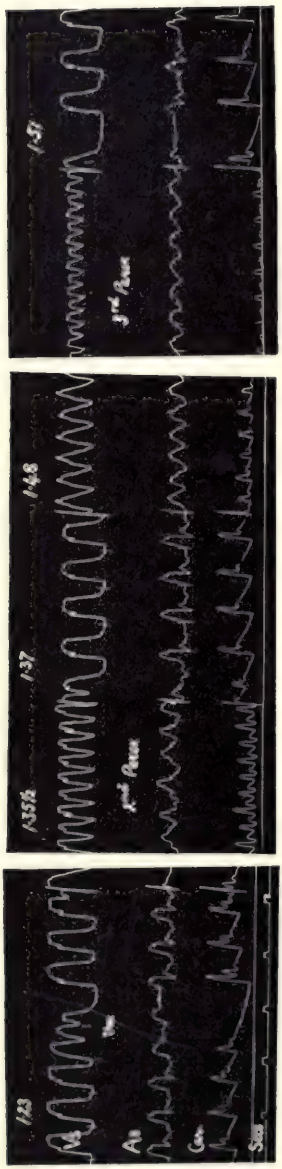

Fig. 78. Three myocardiograms.
(*Ve* = ventricular systole; *As* = auricular systole; *car* = carotid curve.) The right coronary artery was ligatured at 7 minutes past 12 o'clock; the first irregularity was perceived three minutes later. Paroxysms of tachycardia of ventricular origin occurred between 1:20 and 1:50; and at 3:20 the ventricles fibrillated. Portions of the curves are shown. The first shows successive ventricular extrasystoles; the second shows portions of two paroxysms and a strip of the intervening normal rhythm; the third shows a portion of another paroxysm and the succeeding normal rhythm.

human subject are due to ventricular fibrillation. As he points out and emphasises, most of these fatalities occur in the induction stages or at other periods of the administration when the saturation of the blood with chloroform is relatively low. The susceptibility of the cat's heart has recently been confirmed by MacWilliam; Levy has studied the question in such detail that, practically speaking, he can produce the condition and its associated syncope at will. His work upon this subject is a landmark in the history of research upon death under chloroform.

Death in other conditions. Fibrillation of the ventricles is almost certainly the terminal event in many cases of death from lightning (Jex-Blake). Pathological observation also teaches that it is in

this manner that the circulation fails in embolism of a coronary artery. These experiments date from Cohnheim's researches. When a coronary artery, or often when a small branch of such a vessel is obstructed in an animal, there follows within a short space of time a series of remarkable disorders of the heart beat. First the regular rhythm is disturbed by a ventricular extrasystole, then by short runs of these beats occurring successively; a little later they may be so arranged as to constitute short or long paroxysms of tachycardia (Fig. 78); the final event is fibrillation of the ventricle and when this comes the animal dies. It is precisely the same train of events as is seen in chloroform poisoning; a gradual succession of ventricular disorders of ever increasing complexity. The relation of obliteration of a coronary vessel to fibrillation of the ventricles nevertheless is not completely understood. It is probable that it follows acute obstruction only, for it is not a rare thing to find the coronary artery almost or completely occluded by a long standing lesion in human hearts. The coronary vessels are not end-arteries, the anastomoses are clearly displayed by Spalteholz's method and blood is often to be found beyond a complete and old obstruction. If you watch the muscle supplied by a coronary branch upon which a ligature is placed, you will notice that it first becomes livid and, as it loses its function, it balloons with each heart beat; it is at this stage that irregularity of the heart is noticed, if it occurs at all; but often the livid area revives as the anastomosing vessels open up and the disorder of the heart beat vanishes. Obstruction to a small branch may or may not prove fatal in the animal; that it may not prove fatal in man is evidenced by the appearance of fibrotic patches in the muscular wall which may be attributed to arterial occlusion; obstruction of a main coronary in an animal is not necessarily fatal during the period of an experiment, though recovery is rarely seen. I would especially emphasise the possibility that certain of the cases of sudden death in heart disease are due to plug-

ging of vessels supplying relatively small or deeply seated areas of muscle; such vessels are not often examined at autopsy.

Accelerated heart action.

The last cause of syncope which I propose to consider is acceleration of the heart's action. The normal mammalian heart has a wonderful reserve power and capacity of accommodation. You may artificially increase its rate by stimulating it with serial induction shocks over a wide range of rate, without materially influencing the peripheral circulation. The effect of acceleration in the circumstances is to curtail diastole; as a consequence diastolic pressure rises and systolic pressure falls; the mean pressure is maintained. But even in the normal heart

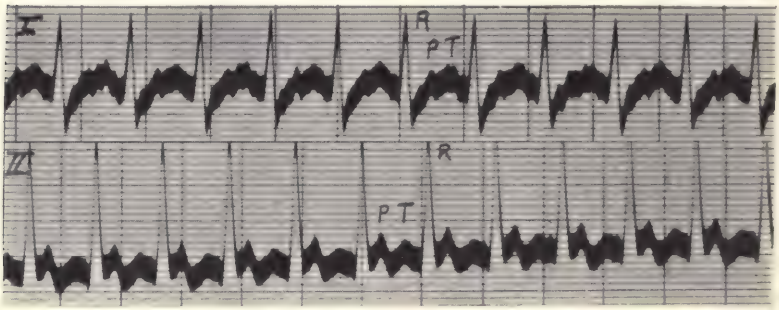

Fig. 79. Electrocardiograms from leads *I* and *II* showing an auricular and a ventricular rate of 270 in a child. Auricular flutter.

there is a limit of this accommodation and, as the rate rises, a time comes when the diastolic periods are so curtailed that filling is incomplete. The mean pressure then falls. If the heart is abnormal or its efficiency is damaged, the effects of acceleration are more speedily felt; a rise of rate, which would create no material disturbance under ordinary conditions, in these circumstances would have profound effects. Some curious examples and contrasts have come to my notice. I recall an instance in which a regular acceleration of the heart's action to 160 and

more per minute had been present for several years; the patient was under my observation for several months, and this rate was constant; yet the disturbance was comparatively slight, consisting only of a sense of exhaustion with and after effort.

Recently a child was brought to me for examination in which the ventricular rate remained at 270-290 during several hours of observation (Fig. 79); the curves from this child were taken while it slept or while, in a waking state, it peacefully took its food. But such rates are very exceptional, and are tolerated only by sound muscle. Where there is muscle damage a rate of 160-200 is rarely tolerated, and higher rates speedily induce signs of grave circulatory embarrassment. This embarrassment comes in the way I have indicated; by a reduction of diastole, arterial pressure is lowered and venous pressure is raised (Fig. 80).

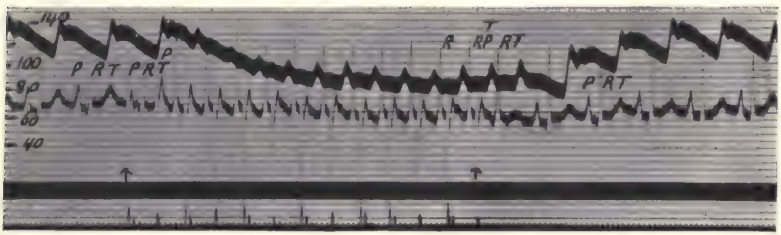

Fig. 80. Hürthle curve of arterial pressure and electrocardiogram. Showing the fall of arterial pressure which occurs when the heart's action is greatly accelerated by stimulation.

Simple paroxysms of regular tachycardia are prone to produce actual attacks of syncope in susceptible subjects; giddiness during the seizures is a common manifestation (Fig. 81). These symptoms are often to be ascribed to lessened cardiac output and the consequent fall of arterial pressure.

I show you an example in Fig. 82 where two short paroxysms of regular tachycardia (rate 200-220 per minute) are recorded; these were accompanied by giddiness, others of longer duration by severe giddiness verging on loss of consciousness; at times the same patient actually fainted. You will notice the lowering

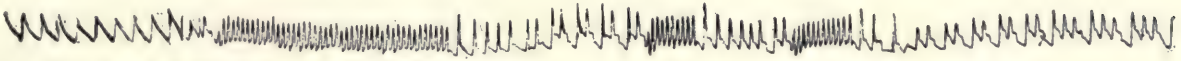

Fig. 81. Brief attacks of paroxysmal tachycardia of auricular origin, accompanied by giddiness.

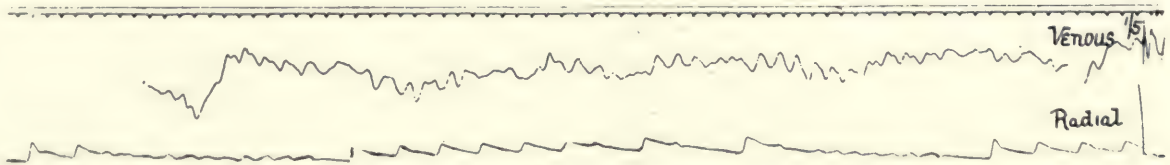

Fig. 82. Two short paroxysms of tachycardia from a patient who complained of attacks of giddiness and fainting attacks. Note the fall of arterial pressure during the progress of the attacks.

of the pulse line, indicating reduction of the blood pressure, as each paroxysm proceeds. Several cases are upon record in which Adams-Stokes syndrome was simulated by paroxysms of this kind, for the beats of the paroxysm failed to force a sufficiency of blood into the arteries and consciousness during the attacks was frequently lost.

Another condition in which giddiness or actual syncope is seen is paroxysmal auricular fibrillation, and the cause is the same in this malady. For the fibrillation in the auricles drives the ventricles at a greatly accelerated rate during the attack, and as a result, mean arterial pressure may be considerably reduced.

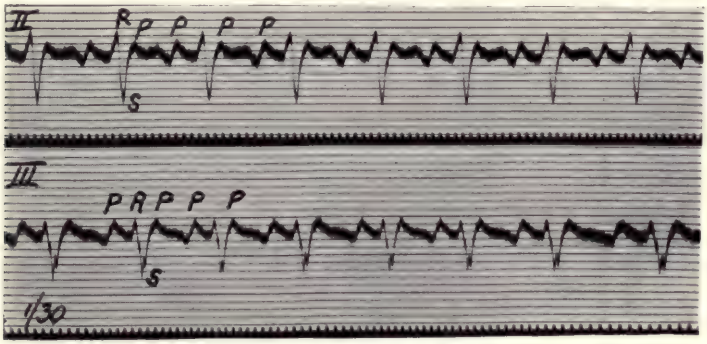

Fig. 83. Electrocardiograms from lead *II* and *III*, showing auricular flutter. The ventricular rate is 165, the auricular rate 330. This patient suffered from syncopal attacks which were proved to result from the assumption of the full auricular rate by the ventricle.

There is a disorder of considerable clinical importance which has but recently been discovered. It is a condition found in adults for the most part, in which the auricles beat at extreme rates, reaching and surpassing 320 per minute. It may be taken as a general rule that in this state, which has been termed *auricular flutter,* the ventricle does not respond to the full auricular rate; it responds to alternate auricular impulses (Fig. 83), and its rate is thus halved. If the auricles beat at 320, the ventricular rate is 160; the ventricular rate of 160 is usually sufficient

materially to embarrass the circulation in these people; how much greater the strain when the full rate is experienced? I question whether any adult heart, normal or abnormal, could long maintain this rate of beating; certain it is that with this heart rate, the cerebral circulation would be grossly insufficient. Now patients who are sufferers from auricular flutter and in whom there is, so to speak, a potential ventricular rate of 300 or more per minute, frequently experience syncopal attacks and it has recently been shown by the graphic method that such attacks are the result of the temporary development of the full ventricular rate. It should be remembered that the auricle is sending forth impulses at 300 per minute and that the ventricle usually refuses half these demands to contract; now and again the full call is answered, the heart rate leaps to its fullest, arterial blood pressure sinks rapidly, the brain is insufficiently supplied, unconsciousness supervenes and is maintained while the ventricle gallops uncurbed.

In the light of these observations, the syncopal attacks of paroxysmal tachycardia receive adequate explanation; death during such attacks — unexpected death in these subjects is not very infrequent — is to be explained by a prolongation of the seizures or, in certain instances, may be, to the intervention of another disorder which we have already considered, namely, fibrillation of the ventricles.

Gentlemen, the facts which I have now related to you constitute our chief knowledge of the causes of cardiac syncope and unexpected death in heart patients. There are still evident gaps to fill; gaps which will be filled in the near future. My purpose has been not only to record our present knowledge in this single direction but to point to the trend of modern observation; by example, to attempt to indicate how clear relations may be established between clinical and laboratory findings; to illustrate the advantages of precise methods of study; to ask your agreement that medicine may be treated as an exact

science, in which the simple facts of our experience may be arranged and sorted out into the compartments of cause and effect, in which a careful and deliberate discrimination between these facts and hypotheses may play a prominent and appropriate part in our processes of thought; to ask your support for the belief that the proved cause of a clinical symptom, however rare such cause may be, is of infinitely greater consequence to us than a hundred plausible suggestions whose validity is unsupported by the evidence of observation.

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